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Welcome to STN International! Enter x:x

LOGINID:SSSPTA1616BSK

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 4	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 5	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 6	FEB 22	Updates in EPFULL; IPC 8 enhancements added
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NEWS 8	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
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NEWS 16	MAY 10	CA/CAplus enhanced with 1900-1906 U.S. patent records
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NEWS 19	MAY 30	IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2
NEWS 20	MAY 30	The F-Term thesaurus is now available in CA/CAplus
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NEWS EXPRESS		FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT http://download.cas.org/express/v8.0-Discover/
NEWS HOURS		STN Operating Hours Plus Help Desk Availability
NEWS LOGIN		Welcome Banner and News Items
NEWS IPC8		For general information regarding STN implementation of IPC 8
NEWS X25		X.25 communication option no longer available after June 2006

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:45:08 ON 22 JUN 2006

=> file reg

COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION
FULL ESTIMATED COST | 0.21 | 0.21

FILE 'REGISTRY' ENTERED AT 17:45:16 ON 22 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 JUN 2006 HIGHEST RN 888750-16-1
DICTIONARY FILE UPDATES: 21 JUN 2006 HIGHEST RN 888750-16-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

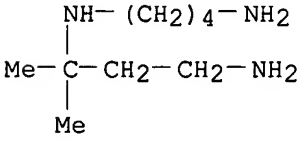
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> s methylspermidine
L1 5 METHYLSPERMIDINE

=> d 1-5

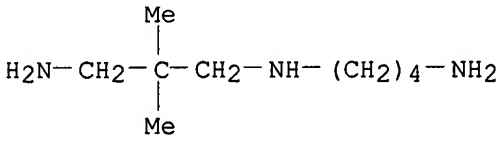
L1 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 105103-53-5 REGISTRY
ED Entered STN: 08 Nov 1986
CN 1,3-Butanediamine, N3-(4-aminobutyl)-3-methyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **3,3-Dimethylspermidine**
FS 3D CONCORD
MF C9 H23 N3
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 105090-79-7 REGISTRY
ED Entered STN: 08 Nov 1986
CN 1,4-Butanediamine, N-(3-amino-2,2-dimethylpropyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **2,2-Dimethylspermidine**
FS 3D CONCORD
MF C9 H23 N3
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
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CN 1,3-Butanediamine, N1-(4-aminobutyl)-3-methyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
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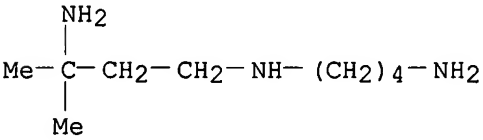
FS 3D CONCORD
MF C9 H23 N3
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER
(*File contains numerically searchable property data)

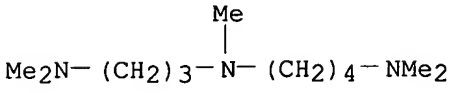


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 54443-84-4 REGISTRY
ED Entered STN: 16 Nov 1984
CN 1,4-Butanediamine, N-[3-(dimethylamino)propyl]-N,N',N'-trimethyl- (9CI)
(CA INDEX NAME)
OTHER NAMES:
CN **N-Permethylspermidine**
FS 3D CONCORD
MF C12 H29 N3
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS

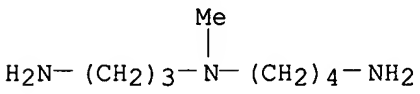
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 51460-23-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **N1-Methylspermidine**
FS 3D CONCORD
DR 94721-33-2
MF C8 H21 N3
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

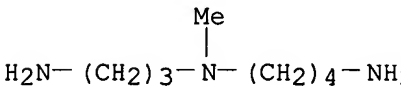
27 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
27 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 20 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:72480 CAPLUS
DOCUMENT NUMBER: 102:72480
TITLE: Treatment with α-difluoromethylornithine plus a spermidine analog leads to spermine depletion and growth inhibition in cultured L1210 leukemia cells
AUTHOR(S): Casero, Robert A., Jr.; Bergeron, Raymond J.; Porter, Carl W.
CORPORATE SOURCE: Roswell Park Mem. Inst., New York State Dep. Health, Buffalo, NY, 14263, USA
SOURCE: Journal of Cellular Physiology (1984), 121(3), 476-82
CODEN: JCLLAX; ISSN: 0021-9541
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Spermine (Spm) [71-44-3] depletion was accomplished by treating cultured L1210 cells for 96 h with α-difluoromethylornithine (DFMO) [70052-12-9] and an analog of spermidine (Spd) such as aminopropylcadaverine [56-19-9], N4-methylSpd [**94721-33-2**], N4-ethylSpd [94721-34-3], or homoSpd [4427-76-3]. DFMO, a specific inhibitor of ornithine decarboxylase, halts continued polyamine biosynthesis and the Spd analog serves as a functional substitute for Spd. Thus, while the Spd analog fulfills the role(s) of Spd in cell proliferation, Spm becomes steadily depleted. In cells treated with DFMO plus the analog, aminopropylcadavarine, Spm pools decline steadily and growth inhibition occurs after 48 h (when Spm pools decline to 60% of control). By 96 h, Spm is .apprx.15% of control and growth is <30%. Prevention studies with exogenous polyamines confirm a causal relationship between Spm depletion and growth inhibition. The critical levels of polyamines for cell proliferation to take place were found to be 30% of control for Spd and 60% for Spm. The use of DFMO plus a Spd analog is proposed as a system for studying the cellular consequences of Spm depletion. Spd depletion can be achieved for comparison purposes by treating cells with DFMO alone.

IT **51460-23-2**
RL: BIOL (Biological study)
(leukemia inhibition by difluoromethylornithine and, spermine depletion in relation to)

RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



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NEWS LOGIN		Welcome Banner and News Items
NEWS IPC8		For general information regarding STN implementation of IPC 8
NEWS X25		X.25 communication option no longer available after June 2006

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 17:45:08 ON 22 JUN 2006

=> file reg

COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION
FULL ESTIMATED COST | 0.21 | 0.21

FILE 'REGISTRY' ENTERED AT 17:45:16 ON 22 JUN 2006

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 JUN 2006 HIGHEST RN 888750-16-1
DICTIONARY FILE UPDATES: 21 JUN 2006 HIGHEST RN 888750-16-1

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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=> s methylspermidine
L1 5 METHYLSPERMIDINE

=> d 1-5

L1 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 105103-53-5 REGISTRY
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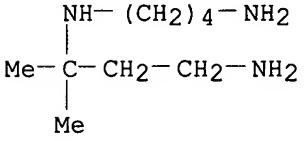
FS 3D CONCORD
MF C9 H23 N3
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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L1 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
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CN 1,4-Butanediamine, N-(3-amino-2,2-dimethylpropyl)- (9CI) (CA INDEX NAME)
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CI COM
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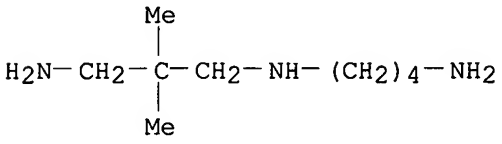

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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L1 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
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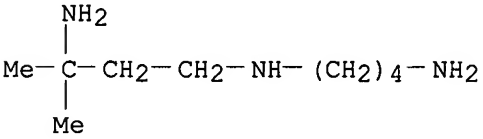
FS 3D CONCORD
MF C9 H23 N3
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
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(CA INDEX NAME)
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MF C12 H29 N3
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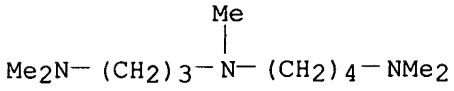
· (*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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OTHER NAMES:
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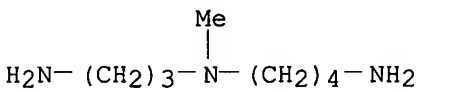
FS 3D CONCORD
DR 94721-33-2
MF C8 H21 N3
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

27 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
27 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus biosis embase

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	15.58	15.79

FILE 'CAPLUS' ENTERED AT 17:47:00 ON 22 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

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Copyright (c) 2006 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 17:47:00 ON 22 JUN 2006
Copyright (c) 2006 Elsevier B.V. All rights reserved.

=> s l12 or methylspermidine
L12 NOT FOUND
The L-number entered could not be found. To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l1 or methylspermidine
L2 99 L1 OR METHYLSPERMIDINE

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 61 DUP REM L2 (38 DUPLICATES REMOVED)

=> focus
PROCESSING COMPLETED FOR L3
L4 61 FOCUS L3 1-

=> s l4/thur
QUALIFICATION NOT VALID FOR L***
Field code qualifications can only be applied to text terms.

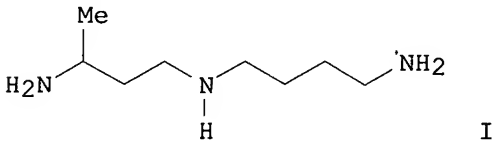
=> d ibib abs hitstr 1-61

L4 ANSWER 1 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:344880 CAPLUS
DOCUMENT NUMBER: 125:28430
TITLE: Interactions of spermidine and **methylspermidine** with DNA studied by nuclear magnetic resonance self-diffusion measurements
AUTHOR(S): Andreasson, Bo; Nordenskioeld, Lars; Schultz, Johan
CORPORATE SOURCE: Division of Physical Chemistry, University of Stockholm, Stockholm, S-10691, Swed.
SOURCE: Biophysical Journal (1996), 70(6), 2847-2856
CODEN: BIOJAU; ISSN: 0006-3495
PUBLISHER: Biophysical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The NMR pulsed field gradient self-diffusion method has been used to study the self-diffusion of the polyamine spermidine and the polyamine analog **methylspermidine** (completely N-methylated spermidine). The self-diffusion coefficient, D, was measured in solns. of calf thymus DNA prepared from nucleosome core particles (with an average length of 120 base pairs) as a function of the concentration ratio of polyamine to DNA phosphate. A study of the self-diffusion quotient, D/Do (where Do is the diffusion coefficient for free polyamine, not associated with DNA), in addns. of spermidine and **methylspermidine** to solns. of NaDNA/NaCl, gave almost identical results with complete association of polyamine to DNA in the initial part of the titrns., indicating similar affinities for DNA. A large influence on the measured self-diffusion coeffs. was detected for **methylspermidine** in NaDNA solns. with different concns. of NaCl, which shows a considerable salt effect on the polyamine-DNA association No notable differences in D/Do for **methylspermidine** were observed in competitive titrns. of solns. of Li- and NaDNA, indicating that sodium and lithium ions behave similarly in their interactions with DNA. In titration expts. of **methylspermidine** into MgDNA solution, the results showed that the polyamine association is less effective than in the case of NaDNA, because of competition from magnesium binding to DNA. Comparisons with calcns. based on the electrostatic Poisson-Boltzmann cell model were performed. It is suggested that the interaction is primarily of electrostatic nature, with no binding to specific sites on the DNA mol.

L4 ANSWER 2 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:54664 CAPLUS
DOCUMENT NUMBER: 118:54664
TITLE: Localized interaction of the polyamine **methylspermidine** with double-helical DNA as monitored by proton NMR self-diffusion measurements
AUTHOR(S): Andreasson, Bo; Nordenskioeld, Lars; Braunlin, William H.; Schultz, Johan; Stilbs, Peter
CORPORATE SOURCE: Div. Phys. Chem., Univ. Stockholm, Stockholm, S-10691, Swed.
SOURCE: Biochemistry (1993), 32(3), 961-7
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 1H NMR pulsed field gradient self-diffusion method has been used to measure the diffusion coefficient of the polyamine analog **methylspermidine** (completely N-methylated spermidine) in DNA solution, as a function of the concentration ratio of **methylspermidine** to DNA phosphate. Three different DNA's have been investigated: d(GC)4 (8 base pairs), core length calf thymus DNA (.apprx.120 base pairs), and

sonicated high mol. weight calf thymus DNA (average 7500 base pairs). For a constant ratio of **methylspermidine** to DNA phosphate, the diffusion coefficient decreases with increasing DNA length. Moreover, at low concentration ratios the diffusion coefficient of **methylspermidine** approaches a limiting value that is close to that of the DNA mol. The exptl. data are well reproduced by a two-state diffusion model. In this model the diffusion coefficient of the polyamine is a population-weighted average of polyamine associated with DNA (with a diffusion coefficient given by that of the DNA mol.) and polyamine free in solution

L4 ANSWER 3 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:642169 CAPLUS
DOCUMENT NUMBER: 141:395701
TITLE: A New Synthesis of α- **Methylspermidine**
AUTHOR(S): Grigorenko, N. A.; Vepsalainen, J.; Jarvinen, A.; Keinanen, T. A.; Alhonen, L.; Janne, J.; Kritsyn, A. M.; Khomutov, A. R.
CORPORATE SOURCE: Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, 119991, Russia
SOURCE: Russian Journal of Bioorganic Chemistry (Translation of Bioorganicheskaya Khimiya) (2004), 30(4), 396-399
CODEN: RJBCET; ISSN: 1068-1620
PUBLISHER: MAIK Nauka/Interperiodica Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:395701
GI



I

AB A five-step synthesis of α- **methylspermidine** (1,8-diamino-5-azanonane, I·3 HCl), the first polyamine analog preventing pathol. consequences of spermidine depletion in transgenic rats overproducing spermine/spermidine N1-acetyltransferase (no data), from Et 3-aminobutyrate was achieved in a high overall yield.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:688737 CAPLUS
DOCUMENT NUMBER: 144:274446
TITLE: Synthesis of (R)- and (S)-isomers of 1-**methylspermidine**
AUTHOR(S): Grigorenko, Nikolay A.; Vepsalainen, Jouko; Jarvinen, Aki; Keinanen, Tuomo; Alhonen, Leena; Janne, Juhani; Khomutov, Alex R.
CORPORATE SOURCE: V.A. Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, 119991, Russia
SOURCE: Mendeleev Communications (2005), (4), 142-143
CODEN: MENCEX; ISSN: 0959-9436
PUBLISHER: Russian Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Previously unknown (R)- and (S)-isomers of 1,8-diamino-5-azanonane were prepared starting from (R)- and (S)-2-aminopropanols.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:627393 CAPLUS
DOCUMENT NUMBER: 121:227393
TITLE: The role of hypusine depletion in cytostasis induced

by S-adenosyl-L-methionine decarboxylase inhibition: new evidence provided by 1-**methylspermidine** and 1,12-dimethylspermine

AUTHOR(S): Byers, Timothy L.; Lakanen, John R.; Coward, James K.; Pegg, Anthony E.

CORPORATE SOURCE: Department of Cell and Molecular Physiology, M.S. Hershey Medical Center, Hershey, PA, 17033, USA

SOURCE: Biochemical Journal (1994), 303(2), 363-8
CODEN: BIJOAK; ISSN: 0264-6021

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The abilities of the natural polyamines, spermidine and spermine, and of the synthetic analogs, 1-**methylspermidine** and 1,12-dimethylspermine, to reverse the effects of the S-adenosyl-L-methionine decarboxylase inhibitor 5'-{[(Z)-4-aminobut-2-enyl]methylamino}-5'-deoxyadenosine (AbeAdo) on L1210-cell growth were studied. L1210 cells were exposed to AbeAdo for 12 days to induce cytostasis and then exposed to spermidine, spermine, 1-**methylspermidine** or 1,12-dimethylspermine in the continued presence of AbeAdo. AbeAdo-induced cytostasis was overcome by the natural polyamines, spermidine and spermine. The cytostasis was also reversed by 1-**methylspermidine**. 1,12-Dimethylspermine had no effect on the AbeAdo-induced cytostasis of chronically treated cells, although it was active in permitting growth of cells treated with the ornithine decarboxylase inhibitor, α-difluoromethylornithine. The initial 12-day exposure to AbeAdo elevated intracellular putrescine levels, depleted intracellular spermidine and spermine, and resulted in the accumulation of unmodified eukaryotic translation initiation factor 5A (eIF-5A). Exposure of these cells to exogenous spermidine, which is the natural substrate for deoxyhypusine synthase, resulted in a decrease in the unmodified eIF-5A content. 1-**Methylspermidine**, which was found to be a substrate of deoxyhypusine synthase in vitro, also decreased the levels of unmodified eIF-5A in the AbeAdo-treated cells. Although spermine is not a substrate of deoxyhypusine synthase, spermine was converted into spermidine in the L1210 cells, and spermine addition to AbeAdo-treated cells resulted in the appearance of both intracellular spermine and spermidine and in the decrease in unmodified eIF-5A. Exogenous 1,12-dimethylspermine, which was not metabolized to spermine or to 1-**methylspermidine** and was not a substrate of deoxyhypusine synthase in vitro, did not decrease levels of unmodified eIF-5A. The finding that AbeAdo-induced cytostasis was only reversed by polyamines and polyamine analogs that result in the formation of hypusine or an analog in eIF-5A is consistent with the hypothesis (Byers, T. L., 1993) that AbeAdo-induced cytostasis is due to the depletion of the hypusine-containing form of eIF-5A, which is secondary to the depletion of spermidine by inhibition of S-adenosyl-L-methionine decarboxylase.

L4 ANSWER 6 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1974:83363 CAPLUS

DOCUMENT NUMBER: 80:83363

TITLE: Synthesis of maytenine, N-**methylspermidine**, and N-methylmaytenine

AUTHOR(S): Schlitter, Emil; Spitaler, Ulrich; Weber, Nikolaus

CORPORATE SOURCE: Pharmakol. Inst., Univ. Heidelberg, Heidelberg, Fed. Rep. Ger.

SOURCE: Helvetica Chimica Acta (1973), 56(3), 1097-9
CODEN: HCACAV; ISSN: 0018-019X

DOCUMENT TYPE: Journal

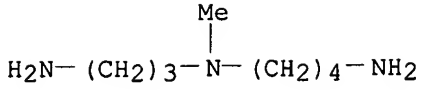
LANGUAGE: German

AB Reaction of H2N(CH2)3NH(CH2)4NH2 (spermidine) with PhCH:CHCOCl (I) in Ba(OH)2-EtOH gave 2.8% trans,trans-PhCH:CHCONH(CH2)3NR(CH2)4NHCOCH:CHPh (II, R = H) (maytenine). Hydrogenation of NCCH2CH2NMe(CH2)3CN over Raney Ni gave 72% H2N(CH2)3NMe(CH2)4NH2, which reacted with I in benzene to give 65% II (R = Me).

IT **51460-23-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 51460-23-2 CAPLUS

CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



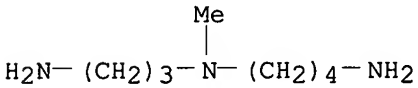
L4 ANSWER 7 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:105949 CAPLUS
DOCUMENT NUMBER: 116:105949
TITLE: α-Methyl polyamines: metabolically stable spermidine and spermine mimics capable of supporting growth in cells depleted of polyamines
AUTHOR(S): Lakanen, John R.; Coward, James K.; Pegg, Anthony E.
CORPORATE SOURCE: Dep. Chem., Univ. Michigan, Ann Arbor, MI, 48109-1055, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(4), 724-34
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to assess the tolerance of the target enzyme spermine synthase for α-substituents on the aminopropyl moiety of the substrate spermidine, 1-**methylspermidine** (I) was synthesized. I is a poor substrate for spermine synthase and is not a substrate for spermidine N1-acetyltransferase, suggesting that α-methylated polyamines might be metabolically stable and therefore useful tools for studying polyamine effects in intact cells. On the basis of initial cellular results with I, 1-methylspermine (II) and 1,12-dimethylspermine (III) were also synthesized. When added to cells (L1210, SV-3T3, or HT29) depleted of both putrescine and spermidine by prior treatment with α-(difluoromethyl)ornithine (IV), these α-methylated polyamines were able to restore cell growth to that observed in the absence of IV. In accord with the enzyme data noted above, metabolic studies indicated a slow conversion of I to II, but no metabolism of III in these cells. It was concluded from these results that the α-methylated polyamines are able to substitute for the natural polyamines, spermidine and spermine in critical biochem. processes which involve polyamines for continued cell growth. In accord with the hypothesis, preliminary data indicate that I and III are as effective as spermidine and spermine, resp., in promoting the conversion of B-DNA to Z-DNA.

L4 ANSWER 8 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:441859 CAPLUS
DOCUMENT NUMBER: 123:4259
TITLE: Enzymic aminopropylation of certain secondary amines
AUTHOR(S): Shirahata, Akira; Hosoda, harumi; Takahashi, Norio; Beppu, Takanobu; Niitsu, Masaru; Samejima, Keijiro
CORPORATE SOURCE: Dep. Anal. Chem., Josai Univ., Saitama, 350-02, Japan
SOURCE: Biological & Pharmaceutical Bulletin (1995), 18(2), 355-9
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two unusual aminopropyl acceptors found in a survey of putrescine binding sites of mammalian spermidine synthase, N-methylputrescine and 4-aminomethylpiperidine, were examined for their aminopropyl derivs. Studies under in vitro incubation conditions suggested that the aminopropyl derivs. of the secondary amine of N-methylputrescine and 4-aminomethylpiperidine, N4-**methylspermidine** and 1-N-(3-aminopropyl)-4-aminomethylpiperidine, and of the primary amine of N-methylputrescine and 4-aminomethylpiperidine, N8-**methylspermidine** and 4-[N-(3-aminopropyl)aminomethyl]piperidine, resp., were biosynthesized by rat spermidine synthase. Studies on the cell culture system of cultured rat hepatoma (HTC) cells treated with α-difluoromethylornithine, an ornithine decarboxylase inhibitor, clearly showed the presence of N-**methylspermidine** and N8-**methylspermidine** when N-methylputrescine was administered, and

1-N-(3-aminopropyl)-4-aminomethylpiperidine and 4-[N-(3-aminopropyl)aminomethyl]piperidine when 4-aminomethylpiperidine was administered, with no detection of putrescine or spermidine. These results suggested that mammalian spermidine synthase can transfer the aminopropyl moiety of decarboxylated S-adenosylmethionine to certain secondary amines in living cells.

IT **51460-23-2P**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); MFM (Metabolic formation); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(enzymic aminopropylation of certain secondary amines by spermidine synthase)

RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)

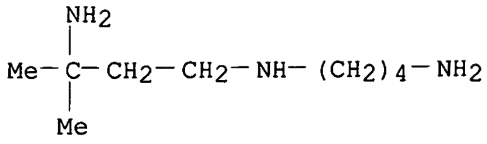


L4 ANSWER 9 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:391 CAPLUS
DOCUMENT NUMBER: 118:391
TITLE: Cytostasis induced in L1210 murine leukemia cells by the S-adenosyl-L-methionine decarboxylase inhibitor 5'-{[(Z)-4-amino-2-butenyl]methylamino}-5'-deoxyadenosine may be due to hypusine depletion
AUTHOR(S): Byers, Timothy L.; Ganem, Bruce; Pegg, Anthony E.
CORPORATE SOURCE: Dep. Cell. Mol. Physiol., M.S. Hershey Med. Cent., Hershey, PA, 17033, USA
SOURCE: Biochemical Journal (1992), 287(3), 717-24
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English

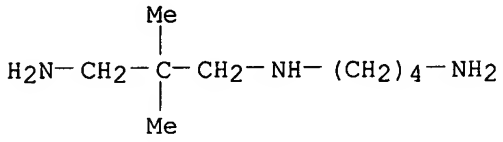
AB The effects of inhibition of the capacity to form spermidine and spermine on cell growth were investigated in murine leukemia L1210 cells using 5'-{[(Z)-4-amino-2-butenyl]methylamino}-5'-deoxyadenosine (MDL 73811, AbeAdo), an enzyme-activated irreversible inhibitor of S-adenosyl-L-methionine decarboxylase. Putrescine levels were increased 80-fold, and spermidine and spermine levels were greatly reduced after a 3-day exposure to the maximal ID of 10 μM AbeAdo. Addition of AbeAdo to the culture medium inhibited the growth of L1210 cells measured 3 days later in a concentration-dependent manner, but, even at the maximally effective concentration of 10 μM, the exposure to AbeAdo was not immediately cytostatic. The growth rate of L1210 cells chronically exposed to 10 μM AbeAdo declined steadily until day 12, when the cells stopped growing. L1210 cells exposed to AbeAdo for 12 days could not be rescued from the cytostasis by removal of the drug from the culture, but could be rescued by the exposure to exogenous spermidine or spermine, indicating that the growth-inhibitory effects of AbeAdo were a result of spermidine and/or spermine depletion. Elevated intracellular putrescine levels in AbeAdo-treated cells may have sustained limited growth in the absence of physiol. levels of spermidine and spermine until certain critical and specific physiol. role(s) fulfilled by spermidine and/or spermine became deficient and caused cytostasis. N-(3-Aminopropyl)-1,4-diamino-cis-but-2-ene, a spermidine analog substrate for deoxyhypusine synthase, was able to mimic the effects of spermidine in reversing the AbeAdo-induced cytostasis. Spermidine analogs such as 5,5-dimethylspermidine, which are not substrates for deoxyhypusine synthase, were not active in this way. The formation of hypusine in the protein synthesis initiation factor eIF-5A may be a critical role of spermidine essential for cell growth.

IT **105090-74-2**, 1,1-Dimethylspermidine **105090-79-7**, 2,2-Dimethylspermidine **105103-53-5**, 3,3-Dimethylspermidine
RL: BIOL (Biological study)
(cytostatic effects of MDL-73811 and, mechanism of)

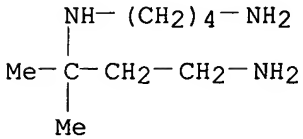
RN 105090-74-2 CAPLUS
CN 1,3-Butanediamine, N1-(4-aminobutyl)-3-methyl- (9CI) (CA INDEX NAME)



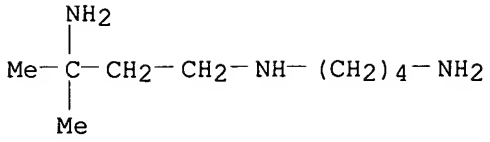
RN 105090-79-7 CAPLUS
CN 1,4-Butanediamine, N-(3-amino-2,2-dimethylpropyl)- (9CI) (CA INDEX NAME)



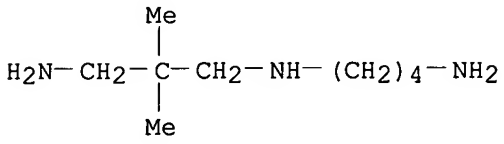
RN 105103-53-5 CAPLUS
CN 1,3-Butanediamine, N3-(4-aminobutyl)-3-methyl- (9CI) (CA INDEX NAME)



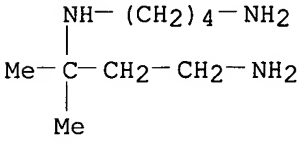
L4 ANSWER 10 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:568108 CAPLUS
DOCUMENT NUMBER: 109:168108
TITLE: Studies of non-metabolizable polyamines that support growth of SV-3T3 cells depleted of natural polyamines by exposure to α-difluoromethylornithine
AUTHOR(S): Nagarajan, Srinivasan; Ganem, Bruce; Pegg, Anthony E.
CORPORATE SOURCE: Baker Lab., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Biochemical Journal (1988), 254(2), 373-8
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A number of synthetic polyamine derivs. that included 5 achiral gem-dimethylspermidines and 2 analogous tetra-Me spermines were tested for their abilities to serve as substrates for enzymes metabolizing polyamines and for their capacities to substitute for the natural polyamines in cell growth. None of the compds. were effective substrates for spermine synthase, and only 1, i.e., 8,8-dimethylspermidine, was a substrate for spermidine/spermine N1-acetyltransferase. However, all of the spermidine derivs. and 1,1,12,12-tetramethylspermine were able to support the growth of SV-3T3 cells in which endogenous polyamine synthesis was prevented by the addition of α-difluoromethylornithine. Apparently, either spermidine or spermine or spermine can support cell growth without the need for metabolic interconversion. In contrast with the result with 1,1,12,12-tetramethylspermine, 3,3,10,10-tetramethylspermine did not restore growth of polyamine-depleted SV-3T3 cells. Comparison of the properties of these derivs. may prove valuable in understanding the physiol. role of polyamines.
IT **105090-74-2 105090-79-7 105103-53-5**
RL: BIOL (Biological study)
(cell growth induction by)
RN 105090-74-2 CAPLUS
CN 1,3-Butanediamine, N1-(4-aminobutyl)-3-methyl- (9CI) (CA INDEX NAME)



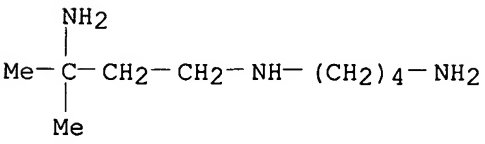
RN 105090-79-7 CAPLUS
CN 1,4-Butanediamine, N-(3-amino-2,2-dimethylpropyl)- (9CI) (CA INDEX NAME)



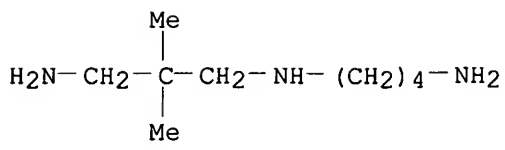
RN 105103-53-5 CAPLUS
CN 1,3-Butanediamine, N3-(4-aminobutyl)-3-methyl- (9CI) (CA INDEX NAME)



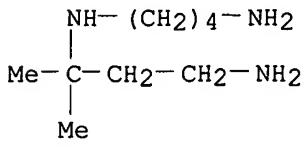
L4 ANSWER 11 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:49851 CAPLUS
DOCUMENT NUMBER: 106:49851
TITLE: Chemistry of naturally occurring polyamines. 10. Nonmetabolizable derivatives of spermine and spermidine
AUTHOR(S): Nagarajan, Srinivasan; Ganem, Bruce
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Journal of Organic Chemistry (1986), 51(25), 4856-61
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 106:49851
AB The synthesis of five gem-dimethylspermidines, e.g., H2NCMe2CH2CH2NH(CH2)4NH2, and the 2 spermine analogs H2NCMe2CH2CH2NH(CH2)4NHCH2CH2CMe2NH2 and H2NCH2CH2CMe2NH(CH2)4NHCMe2CH2CH2NH2 was described. These compds. were designed to act as polyamine oxidase inhibitors and to serve as useful probes of complex polyamine biosynthesis.
IT **105090-74-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and cyclization with formaldehyde)
RN 105090-74-2 CAPLUS
CN 1,3-Butanediamine, N1-(4-aminobutyl)-3-methyl- (9CI) (CA INDEX NAME)



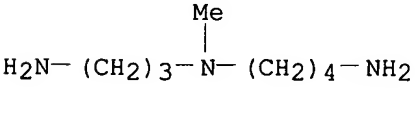
IT **105090-79-7P 105103-53-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 105090-79-7 CAPLUS
CN 1,4-Butanediamine, N-(3-amino-2,2-dimethylpropyl)- (9CI) (CA INDEX NAME)



RN 105103-53-5 CAPLUS
CN 1,3-Butanediamine, N3-(4-aminobutyl)-3-methyl- (9CI) (CA INDEX NAME)



L4 ANSWER 12 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:281914 CAPLUS
DOCUMENT NUMBER: 129:38778
TITLE: Unusual polyamines in aquatic plants: the occurrence of homospermidine, norspermidine, thermospermine, norspermine, aminopropylhomospermidine, bis(aminopropyl)ethanediamine, and **methylspermidine**
AUTHOR(S): Hamana, Koei; Niitsu, Masaru; Samejima, Keijiro
CORPORATE SOURCE: School of Health Sciences, Faculty of Medicine, Gunma University, Gunma, 371, Japan
SOURCE: Canadian Journal of Botany (1998), 76(1), 130-133
CODEN: CJBOAW; ISSN: 0008-4026
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Four aquatic plants were tested for the occurrence of unusual polyamines. The leaves of the aquatic plants tested ubiquitously contained homospermidine in addition to usual polyamines such as diaminopropane, putrescine, cadaverine, spermidine, spermine, and agmatine. Brasenia schreberi and Nuphar japonicum belonging to the family Nymphaeaceae contained aminopropylhomospermidine. Norspermidine and norspermine were detected in the blackweed Hydrilla verticillata belonging to Hydrocharitaceae. Thermospermine was detected in Brasenia schreberi. A novel tetraamine, N,N'-bis(3-aminopropyl)-1,2-ethanediamine (NH2(CH2)3NH(CH2)2NH(CH2)3NH2), was discovered in the aquatic plant Nuphar japonicum. This is the first report of the occurrence of N4-**methylspermidine** (NH2(CH2)3N(CH3)(CH2)4NH2) in the water chestnut Trapa natas belonging to the family Hydrocaryaceae.
IT **51460-23-2**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(unusual polyamines in aquatic plants)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:783211 CAPLUS
DOCUMENT NUMBER: 138:331376
TITLE: A Polyamine Analogue Prevents Acute Pancreatitis and

Restores Early Liver Regeneration in Transgenic Rats with Activated Polyamine Catabolism

AUTHOR(S): Raesaenen, Tiina-Liisa; Alhonen, Leena; Sinervirta, Riitta; Keinaenen, Tuomo; Herzig, Karl-Heinz; Suppola, Suvikki; Khomutov, Alex R.; Vepsaelaeinen, Jouko; Jaenne, Juhani

CORPORATE SOURCE: A.I. Virtanen Institute for Molecular Sciences, University of Kuopio, Kuopio, FIN-70211, Finland

SOURCE: Journal of Biological Chemistry (2002), 277(42), 39867-39872
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

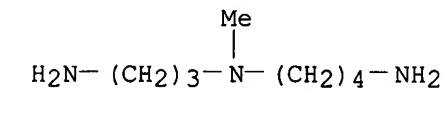
LANGUAGE: English

AB We recently generated a transgenic rat model for acute pancreatitis, which was apparently caused by a massive depletion of pancreatic polyamines spermidine and spermine due to inducible activation of their catabolism (Alhonen, L., Parkkinen, J. J., Keinaenen, T., Sinervirta, R., Herzig, K. H., and Jaenne, J. (2000) Proc. Natl. Acad. Sci. U. S. A. 97, 8290-8295). When subjected to partial hepatectomy, these animals showed striking activation of polyamine catabolism at 24 h postoperatively with a profound decrease in hepatic spermidine and spermine pools and failure to initiate liver regeneration. Here we show that pancreatitis in this model could be totally prevented, as judged by histopathol. and plasma α-amylase activity, by administration of 1-**methylspermidine**, a metabolically stable analog of spermidine. Similarly, the analog, given prior to partial hepatectomy, restored early liver regeneration in the transgenic rats, as indicated by a dramatic increase in the number of proliferating cell nuclear antigen-pos. hepatocytes from about 1% to more than 40% in response to the drug. The present results suggest that the extremely high concentration of spermidine in the pancreas, in fact the highest in the mammalian body, may have a critical role in maintaining organ integrity. The failure to initiate liver regeneration in the absence of sufficient hepatic polyamine pools similarly indicates that polyamines are required for proper commencement of the regenerative process.

IT **51460-23-2**, N1-**Methylspermidine**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamine analog prevents acute pancreatitis and restores early liver regeneration in transgenic rats with activated polyamine catabolism)

RN 51460-23-2 CAPLUS

CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:191841 CAPLUS

DOCUMENT NUMBER: 116:191841

TITLE: Accumulation of polyamine analogs in red blood cells: a potential index of tumor proliferation rate

AUTHOR(S): Moulinoux, Jacques Philippe; Quemener, Veronique; Havouis, Rene; Guille, Francois; Martin, Christian; Seiler, Nikolaus

CORPORATE SOURCE: Groupe Rech. Ther. Anticancereuse, Fac. Med. Rennes I, Rennes, F-35043, Fr.

SOURCE: Anticancer Research (1991), 11(6), 2143-6
CODEN: ANTRD4; ISSN: 0250-7005

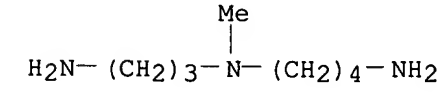
DOCUMENT TYPE: Journal

LANGUAGE: English

AB It has previously been demonstrated that during Lewis lung carcinoma (3LL) growth, red blood cell (RBC) spermidine (Spd) levels change concomitantly

with the tumor volume and [14C]Spd accumulates in proportion with the tumor volume, if [14C]putrescine (Put) is administered. The present study substituted a non-radioactive analog for labeled Put with the aim to perform human studies, should the method prove suitable to quantify malignant cell proliferation intensity. 2-Methylputrescine (2MPut) is an excellent substrate of spermidine synthase and is transformed in vivo into **methylspermidine** (MSpd) and 6-methylspermine. After a single i.p. dose of 2MPu, MSpd accumulated in RBC of mice with 3LL xenografts. The concentration of MSpd correlated directly with tumor progression. No significant amts. of MSpd were found in RBC of normal mice. Thus, 2MPut may become a new tool in tumor diagnostics.

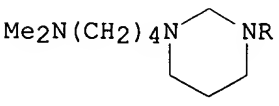
L4 ANSWER 15 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:380810 CAPLUS
DOCUMENT NUMBER: 122:154301
TITLE: Effect of expression of human spermidine/spermine N1-acetyltransferase in Escherichia coli
AUTHOR(S): Parry, Lisa; Lopez-Ballester, Juan; Wiest, Laurie; Pegg, Anthony E.
CORPORATE SOURCE: College of Medicine, Pennsylvania State University, Hershey, PA, 17033, USA
SOURCE: Biochemistry (1995), 34(8), 2701-9
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A plasmid expression vector, pINSAT2, was constructed in order to express spermidine/spermine N1-acetyltransferase (SSAT) in Escherichia coli. Cells transfected with this vector produced large amts. of SSAT, amounting to up to 2% of the soluble protein when iso-Pr β-D-thiogalactopyranoside (IPTG) was added and 0.3% of the soluble protein in the absence of inducer. The growth rate of cells expressing SSAT was reduced, and all of the cellular spermidine was converted to N1-acetylspermidine, much of which was excreted. Putrescine and 1-**methylspermidine**, which is not a substrate for SSAT, could reverse the effects of SSAT expression on growth, but spermidine was only effective when the amount of SSAT expression was limited by omitting the IPTG inducer. The lack of stimulation of growth by spermidine correlated with its complete conversion to N1-acetylspermidine. These results show that N1-acetylspermine is not able to substitute for the unmodified polyamines in supporting growth and suggest that acetylation is a physiol. response to convert excess polyamines to a physiol. inert form which is readily excreted. Cells expressing large amts. of SSAT were much more sensitive to the growth inhibitory action of the antitumor agent N1,N12-bis(ethyl)spermine, supporting the hypothesis that the ability of such bis(ethyl) polyamines to induce SSAT contributes to their antiproliferative actions. SSAT was readily purified to homogeneity from exts. of DH5α cells containing pINSAT2. The purified enzyme had a similar specific activity and Km values for spermine and spermidine as the enzyme purified from human colon cancer cells, suggesting that posttranslational modifications specific to eukaryotes are not needed for enzymic activity. The recombinant SSAT was found to acetylate the drugs 15-deoxyspergualin, 2-[(aminopropyl)amino]ethanethiol, and N-(n-butyl)-1,3-diaminopropane.
IT **51460-23-2**, N1-**Methylspermidine**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(effect of expression of human spermidine/spermine N1-acetyltransferase in Escherichia coli)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



L4 ANSWER 16 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:149929 CAPLUS
DOCUMENT NUMBER: 142:385921
TITLE: Metabolic Stability of α-Methylated Polyamine Derivatives and Their Use as Substitutes for the Natural Polyamines
AUTHOR(S): Jaervinen, Aki; Grigorenko, Nikolay; Khomutov, Alex R.; Hyvoenen, Mervi T.; Uimari, Anne; Vepsaelaeinen, Jouko; Sinervirta, Riitta; Keinaenen, Tuomo A.; Vujcic, Slavoljub; Alhonen, Leena; Porter, Carl W.; Jaenne, Juhani
CORPORATE SOURCE: A. I. Virtanen Institute for Molecular Sciences, University of Kuopio, Kuopio, FIN-70211, Finland
SOURCE: Journal of Biological Chemistry (2005), 280(8), 6595-6601
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Metabolically stable polyamine derivs. may serve as useful surrogates for the natural polyamines in studies aimed to elucidate the functions of individual polyamines. Here we studied the metabolic stability of α- **methylspermidine**, α-methylspermine, and bis-α-methylspermine, which all have been reported to fulfill many of the putative physiol. functions of the natural polyamines. In vivo studies were performed with the transgenic rats overexpressing spermidine/spermine N1-acetyltransferase. α- **Methylspermidine** effectively accumulated in the liver and did not appear to undergo any further metabolism On the other hand, α-methylspermine was readily converted to α- **methylspermidine** and spermidine; similarly, bis-α-methylspermine was converted to α- **methylspermidine** to some extent, both conversions being inhibited by the polyamine oxidase inhibitor N1,N2-bis(2,3-butadienyl)-1,4-butanediamine. Furthermore, we used recombinant polyamine oxidase, spermidine/spermine N1-acetyltransferase, and the recently discovered spermine oxidase in the kinetic studies. In vitro studies confirmed that methylation did not protect spermine analogs from degradation, whereas the spermidine analog was stable. Both α- **methylspermidine** and bis-α-methylspermine overcame the proliferative block of early liver regeneration in transgenic rats and reversed the cytostasis induced by an inhibition of ornithine decarboxylase in cultured fetal fibroblasts.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:120779 CAPLUS
DOCUMENT NUMBER: 94:120779
TITLE: The chemistry of naturally occurring polyamines. Part 3. Synthesis of cytotoxic spermidine metabolites from the soft coral Sinularia brongersmai
AUTHOR(S): Chantrapromma, Kan; McManis, James S.; Ganem, Bruce
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Tetrahedron Letters (1980), 21(27), 2605-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

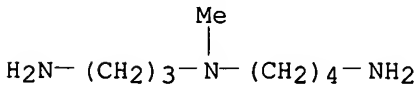


II

AB The preparation of the trimethylspermidine amides Me(CH2)8CMeRCHRCONH(CH2)3NMe(CH2)4NMe2 (I; R2 = trans-bond; R = H) is reported. The hexahydropyrimidine II (R = H), prepared by sequential acetylation, partial

hydrolysis, Eschweiler-Clarke methylation and reduction of H2N(CH2)4NH(CH2)3NH2 (III), underwent condensation with Me(CH2)8CMe:CHCOCl, prepared in 3 steps from Me(CH2)8COMe and (EtO)2P(O)CH2CO2Et, to give II [R = COCH:CMe(CH2)8Me] (IV). IV underwent regiospecific reductive cleavage to give 96% I (R2 = bond), which was catalytically reduced (Pd/C) to I (R = H) (15% overall yield from III).

L4 ANSWER 18 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:666667 CAPLUS
DOCUMENT NUMBER: 138:406725
TITLE: Polyamine structural effects on the induction and stabilization of liquid crystalline DNA: potential applications to DNA packaging, gene therapy and polyamine therapeutics
AUTHOR(S): Saminathan, M.; Thomas, Thresia; Shirahata, Akira; Pillai, C. K. S.; Thomas, T. J.
CORPORATE SOURCE: Department of Medicine, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, New Brunswick, NJ, 08903, USA
SOURCE: Nucleic Acids Research (2002), 30(17), 3722-3731
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB DNA undergoes condensation, conformational transitions, aggregation and resolubilization in the presence of polyamines, pos. charged organic mols. present in all cells. Under carefully controlled environmental conditions, DNA can also transform to a liquid crystalline state in vitro. We undertook the present work to examine the ability of spermidine, N4-**methylspermidine**, spermine, N1-acetylspermine and a group of tetramine, pentamine and hexamine analogs of spermine to induce and stabilize liquid crystalline DNA. Liquid crystalline textures were identified under a polarizing microscope. In the absence of polyamines, calf thymus DNA assumed a diffused, planar cholesteric phase with entrapped bubbles when incubated on a glass slide at 37°C. In the presence of spermidine and spermine, the characteristic fingerprint textures of the cholesteric phase, adopting a hexagonal order, were obtained. The helical pitch was 2.5 μm. The final structures were dendrimeric and crystalline when DNA was treated with spermine homologs and bis(ethyl) derivs. A cholesteric structure was observed when DNA was treated with a hexamine at 37°C. This structure changed to a hexagonal dendrimer with fluidity on prolonged incubation. These data show a structural specificity effect of polyamines on liquid crystalline phase transitions of DNA and suggest a possible physiol. function of natural polyamines.
IT **51460-23-2**
RL: MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamine structural effects on the induction and stabilization of liquid crystalline DNA: potential applications to DNA packaging, gene therapy and polyamine therapeutics)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 61 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:445785 BIOSIS
DOCUMENT NUMBER: PREV200400448161
TITLE: A new synthesis of alpha-**methylspermidine**.
AUTHOR(S): Grigorenko, N. A. [Reprint Author]; Vepsalainen, J.; Jarvinen, A.; Keinanen, T. A.; Alhonen, L.; Janne, J.;

Kritsyn, A. M.; Khomutov, A. R.
CORPORATE SOURCE: VA Engelhardt Mol Biol Inst, Russian Acad Sci, Ul Vavilova 32, Moscow, 119991, Russia
SOURCE: Bioorganicheskaya Khimiya, (July 2004) Vol. 30, No. 4, pp. 441-445. print.
CODEN: BIKHD7. ISSN: 0132-3423.
DOCUMENT TYPE: Article
LANGUAGE: Russian
ENTRY DATE: Entered STN: 17 Nov 2004
Last Updated on STN: 17 Nov 2004

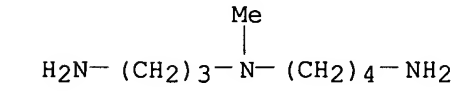
AB A five-step synthesis of a-**methylspermidine** (1,8-diamino-5-azanonane), the first polyamine analogue preventing pathological consequences of spermidine depletion in transgenic rats overproducing spermine/spermidine N1-acetyltransferase, from ethyl 3-aminobutyrate was achieved in a high overall yield.

L4 ANSWER 20 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:72480 CAPLUS
DOCUMENT NUMBER: 102:72480
TITLE: Treatment with α-difluoromethylornithine plus a spermidine analog leads to spermine depletion and growth inhibition in cultured L1210 leukemia cells
AUTHOR(S): Casero, Robert A., Jr.; Bergeron, Raymond J.; Porter, Carl W.
CORPORATE SOURCE: Roswell Park Mem. Inst., New York State Dep. Health, Buffalo, NY, 14263, USA
SOURCE: Journal of Cellular Physiology (1984), 121(3), 476-82
CODEN: JCLLAX; ISSN: 0021-9541
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Spermine (Spm) [71-44-3] depletion was accomplished by treating cultured L1210 cells for 96 h with α-difluoromethylornithine (DFMO) [70052-12-9] and an analog of spermidine (Spd) such as aminopropylcadaverine [56-19-9], N4-methylSpd [**94721-33-2**], N4-ethylSpd [94721-34-3], or homoSpd [4427-76-3]. DFMO, a specific inhibitor of ornithine decarboxylase, halts continued polyamine biosynthesis and the Spd analog serves as a functional substitute for Spd. Thus, while the Spd analog fulfills the role(s) of Spd in cell proliferation, Spm becomes steadily depleted. In cells treated with DFMO plus the analog, aminopropylcadavarine, Spm pools decline steadily and growth inhibition occurs after 48 h (when Spm pools decline to 60% of control). By 96 h, Spm is .apprx.15% of control and growth is <30%. Prevention studies with exogenous polyamines confirm a causal relationship between Spm depletion and growth inhibition. The critical levels of polyamines for cell proliferation to take place were found to be 30% of control for Spd and 60% for Spm. The use of DFMO plus a Spd analog is proposed as a system for studying the cellular consequences of Spm depletion. Spd depletion can be achieved for comparison purposes by treating cells with DFMO alone.

IT **51460-23-2**
RL: BIOL (Biological study)
(leukemia inhibition by difluoromethylornithine and, spermine depletion in relation to)

RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



L4 ANSWER 21 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:252763 CAPLUS
DOCUMENT NUMBER: 135:73053
TITLE: Circular Dichroism and NMR Studies of Metabolically Stable α-Methylpolyamines: Spectral Comparison with Naturally Occurring Polyamines

AUTHOR(S): Varnado, Byron L.; Voci, Christopher J.; Meyer, Lynn M.; Coward, James K.
CORPORATE SOURCE: Departments of Medicinal Chemistry and Chemistry, The University of Michigan, Ann Arbor, MI, 48109-1055, USA
SOURCE: Bioorganic Chemistry (2000), 28(6), 395-408
CODEN: BOCMBM; ISSN: 0045-2068
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three synthetic polyamine analogs, α- **methylspermidine**, α-methylspermine, and α,α'-dimethylspermine, were compared with their naturally occurring counterparts, spermidine and spermine, by two different spectral techniques. The interaction of polyamines with oligodeoxynucleotides was measured by CD in order to monitor the polyamine-induced conversion of right-handed B-DNA to the left-handed Z-form. The methylated analogs were shown to be equally effective as the natural polyamines in inducing the B → Z transition. The pH dependence of the chemical shift of all carbon atoms in each of the five polyamines was measured by 13C-NMR spectroscopy. With the exception of expected changes in chemical shift due to the presence of the α-Me substituents, the chemical shifts and pH dependence of all carbon atoms in the three α-Me polyamines were similar to the corresponding naturally occurring polyamines. The combined data indicate that α-Me polyamines have phys. properties that are very similar to their natural counterparts. The two metabolically stable polyamine analogs, α- **methylspermidine** and α,α'-dimethylspermine, are therefore useful surrogates for spermidine and spermine in the study of numerous polyamine-mediated effects in mammalian cell cultures and can be used in such studies without the requirement for coadministration of amine oxidase inhibitors. (c) 2000 Academic Press.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:487201 CAPLUS
DOCUMENT NUMBER: 131:120600
TITLE: Reduction of hair growth with inhibitors of deoxyhypusine synthase and hydroxylase
INVENTOR(S): Styczynski, Peter; Ahluwalia, Gurpreet S.; Shander, Douglas
PATENT ASSIGNEE(S): Handelman, Joseph H., USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9937277	A1	19990729	WO 1998-US15649	19980727
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6060471	A	20000509	US 1998-10227	19980121
CA 2316826	AA	19990729	CA 1998-2316826	19980727
CA 2316826	C	20030211		
AU 9885982	A1	19990809	AU 1998-85982	19980727
AU 751428	B2	20020815		
BR 9814249	A	20001003	BR 1998-14249	19980727
EP 1049444	A1	20001108	EP 1998-937216	19980727
EP 1049444	B1	20040324		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
AT 262309	E	20040415	AT 1998-937216	19980727

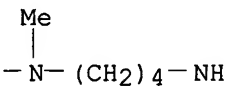
ES 2214719	T3	20040916	ES 1998-937216		19980727
ZA 9806822	A	19990202	ZA 1998-6822		19980730
PRIORITY APPLN. INFO.:			US 1998-10227	A	19980121
			WO 1998-US15649	W	19980727

AB Mammalian hair growth is reduced by applying to the skin an inhibitor of hypusine biosynthetic pathway. Golden Syrian hamster assay showed that 1,8-diaminooctane (deoxyhypusine synthase inhibitor) reduced the hair mass in a dose-dependent manner.

IT **51460-23-2**, N1-**Methylspermidine**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hair growth inhibition by applying inhibitors of hypusine biosynthetic pathway)

RN 51460-23-2 CAPLUS

CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:474505 CAPLUS

DOCUMENT NUMBER: 121:74505

TITLE: Activation of vitamin D receptor of porcine intestine by polyamines

AUTHOR(S): Morishima, Yoshihiro

CORPORATE SOURCE: First Dep. Biochem., Osaka City Univ. Med. Sch., Osaka, Japan

SOURCE: Osaka-shi Igakkai Zasshi (1993), 42(1), 1-16
CODEN: OIGZDE; ISSN: 0386-4103

DOCUMENT TYPE: Journal

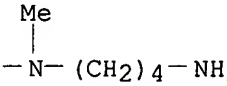
LANGUAGE: Japanese

AB As part of the intracellular action of 1α,25-dihydroxyvitamin D3, vitamin D receptors (VDR) seem to undergo activation before they bind to the specific site on the target gene, vitamin D response element. One group of compds. that might be important for the activation of VDR is the polyamines. In this paper, the effects of polyamines and their analogs on the sedimentation properties and DNA binding activity of VDR extracted from porcine intestinal mucosa are reported. Sucrose d. gradient anal. showed that polyamines decreased the sedimentation coefficient of VDR dose-dependently and increased its DNA binding activity. These findings showed that polyamines can activate VDR in vitro. Among the naturally existing polyamines, spermidine and spermine but not putrescine may be important in the activation of VDR in vivo as well, since both activated VDR at physiol. intracellular concns. Sucrose d. gradient anal. with various polyamine analogs showed that the cationic property of polyamines is important for the change in the sedimentation coefficient of VDR, and that the distance between two pos. charges on the mols. is not important. RNase but not DNase activated VDR dose-dependently, which suggests that dissociation of RNA from VDR is involved in the activation of VDR.

IT **51460-23-2**, N1-**Methylspermidine**
RL: BIOL (Biological study)
(dihydroxyvitamin D3 receptor activation by, in intestine)

RN 51460-23-2 CAPLUS

CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



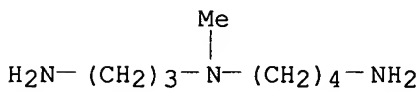
L4 ANSWER 24 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1033676 CAPLUS
DOCUMENT NUMBER: 142:183114
TITLE: Ternary complexes comprising polyphosphoramidate gene carriers with different types of charge groups improve transfection efficiency
AUTHOR(S): Zhang, Peng-Chi; Wang, Jun; Leong, Kam W.; Mao, Hai-Quan
CORPORATE SOURCE: Tissue and Therapeutic Engineering Laboratory, Johns Hopkins Singapore, Singapore, 117597, Singapore
SOURCE: Biomacromolecules (2005), 6(1), 54-60
CODEN: BOMAF6; ISSN: 1525-7797
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To understand the influence of charge groups on transfection mediated by polymer complexes, we have synthesized a series of biodegradable and cationic polyphosphoramidates (PPAs) with an identical backbone but different side chains. Our previous study showed that PPA with a spermidine side chain (PPA-SP) showed high transfection efficiency in culture, whereas PPAs with secondary, tertiary, and quaternary amino groups were significantly less efficient. To investigate whether the coexistence of 1° amino charge groups with 3° and 2° amino charge groups in the DNA/polymer complexes would enhance their transfection efficiency, we evaluated a ternary complex system containing DNA and PPAs with 1° amino groups (PPA-SP) and 3° amino groups (PPA-DMA) and a quaternary complex system containing DNA and PPAs with 1° and 2° and 3° amino groups (PPA-EA/PPA-MEA/PPA-DMA), resp. Ternary complexes mediated 20 and 160 times higher transfection efficiency in COS-7 cells than complexes of DNA with PPA-SP or PPA-DMA alone, resp. Similarly, quaternary complexes exhibited 8-fold higher transfection efficiency than PPA-EA/DNA complexes. The mechanism of enhancement in transfection efficiency by the mixture carriers appears to be unrelated to the particle size, zeta potential, or DNA uptake. The titration characterization and the transfection expts. using a proton pump inhibitor suggested that the enhancement effect is unlikely due to the slightly improved buffering capacity of the mixture over PPA-SP. This approach represented a simple strategy of developing polymeric gene carriers and understanding the mechanisms of polymer-mediated gene transfer.

IT **51460-23-2DP**, reaction products with poly(1,2-propylenephosphonate), complexes with DNA
RL: BSU (Biological study, unclassified); POF (Polymer in formulation); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DNA complexes with polyphosphoramidate mixts. as gene carriers for improved transfection efficiency)

RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

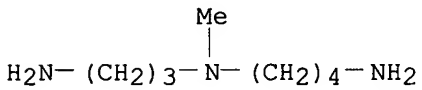
L4 ANSWER 25 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:350532 CAPLUS
DOCUMENT NUMBER: 138:112274
TITLE: Biodegradable polyphosphoramidates as gene carriers: Effect of charge groups on transfection efficiency
AUTHOR(S): Wang, J.; Mao, H.-Q.; Leong, K. W.
CORPORATE SOURCE: Clinical Research Center, Johns Hopkins Singapore, Singapore, 117597, Singapore
SOURCE: Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego,

CA, United States, June 23-27, 2001 (2001), Volume 2, 1119-1120. Controlled Release Society: Minneapolis, Minn.
CODEN: 69CNY8
DOCUMENT TYPE: Conference
LANGUAGE: English

AB To elucidate the important features of polymeric gene carriers, a series of new cationic polyphosphoramidates (PPAs) with an identical backbone but different side chains containing primary to tertiary amino groups were synthesized. These PPA carriers showed different transfection abilities and DNA binding capacities. PPA with a spermidine side chain was the most efficient in several cell lines, while other PPAs only achieved moderate levels of gene expression. Chloroquine significantly enhanced the transfection efficiency. These PPAs were less toxic than PEI and PLL.

IT **51460-23-2DP**, reaction products with polydioxaphospholane
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(charge groups effect on transfection efficiency of biodegradable polyphosphoramidates as gene carriers)

RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:489237 CAPLUS
DOCUMENT NUMBER: 135:71297
TITLE: Polyamines and polyamine derivatives as glycosidase inhibitors and their pharmacological uses, in particular for treating diabetes
INVENTOR(S): Aghajari, Nushin Banu Helene; Robert, Xavier Guy; Haser, Richard Michel
PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique, Fr.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047528	A2	20010705	WO 2000-FR3600	20001220
WO 2001047528	A3	20020620		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2802817	A1	20010629	FR 1999-16409	19991223
FR 2802817	B1	20021011		
CA 2395305	AA	20010705	CA 2000-2395305	20001220
EP 1239863	A2	20020918	EP 2000-990069	20001220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518501	T2	20030610	JP 2001-548121	20001220
US 2003143713	A1	20030731	US 2002-168703	20021024

PRIORITY APPLN. INFO.: FR 1999-16409 A 19991223
WO 2000-FR3600 W 20001220

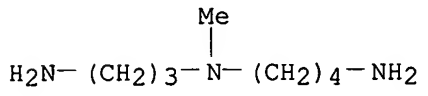
OTHER SOURCE(S): MARPAT 135:71297

AB The invention discloses the use of a polyamine or polyamine derivative for inhibiting the active site of glycosidases converting polysaccharides into sugars, in particular into glucose, in a living organism. The compds. of the invention are useful in the treatment of diabetes.

IT **51460-23-2D**, α-amylase complexes
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(polyamines and polyamine derivs. as glycosidase inhibitors and pharmacol. use, especially for treating diabetes)

RN 51460-23-2 CAPLUS

CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



L4 ANSWER 27 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:143271 CAPLUS

DOCUMENT NUMBER: 130:334252

TITLE: Ionic and Structural Specificity Effects of Natural and Synthetic Polyamines on the Aggregation and Resolubilization of Single-, Double-, and Triple-Stranded DNA

AUTHOR(S): Saminathan, Muthusamy; Antony, Thomas; Shirahata, Akira; Sigal, Leonard H.; Thomas, Thresia; Thomas, T. J.

CORPORATE SOURCE: Departments of Medicine Environmental and Community Medicine Molecular Genetics and Microbiology and Pediatrics, Environmental and Occupational Health Sciences Institute and The Cancer Institute of New Jersey, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, New Brunswick, NJ, 08903, USA

SOURCE: Biochemistry (1999), 38(12), 3821-3830
CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

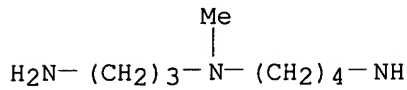
LANGUAGE: English

AB DNA condensation, precipitation, and aggregation are related phenomena involving DNA-DNA interactions in the presence of multivalent cations, and studied for their potential implications in DNA packaging in the cell. Recent studies have shown that the condensation/aggregation is a prerequisite for the cellular uptake of DNA for gene therapy applications. To elucidate the ionic and structural factors involved in DNA aggregation, we studied the precipitation and resolubilization of high mol. weight and sonicated calf thymus DNA, two therapeutic oligonucleotides, and poly(dA)·2Poly(dT) triplex DNA in the presence of the tetravalent polyamine spermine using a centrifugation assay, Tm measurements, and CD spectroscopy. The ability of spermine to provoke DNA precipitation was in the following order: triplex DNA > duplex DNA > single-stranded DNA. In contrast, their resolubilization at high polyamine concns. followed a reverse order. The effective concentration of spermine to precipitate DNA increased with Na+ in the medium. Tm data indicated the DNA stabilizing effect of spermine even in the resolubilized state. CD spectroscopy revealed a series of sequential conformational alterations of duplex and triplex DNA, with the duplex form regaining the B-DNA conformation at high concns. (.apprx.200 mM) of spermine. The triplex DNA, however, remained in a Ψ-DNA conformation in the resolubilized state. Chemical structural specificity effects were exerted by spermidine and spermine analogs in precipitating and resolubilizing sonicated calf thymus DNA, with N4-Me substitution of spermidine and a heptamethylene separation of the imino groups of spermine having the maximal difference in the precipitating ability of the analogs compared to spermidine and spermine, resp. Therapeutically important bis(ethyl) substitution reduced the precipitating

ability of the analogs compared to spermine. The effect of the cationicity of polyamines was evident with the pentamines being much more efficacious than the tetramines and triamines. These results provide new insights into the mechanism of DNA precipitation by polyamines, and suggest the importance of polyamine structure in developing gene delivery vehicles for therapeutic applications.

IT **51460-23-2**
RL: BPR (Biological process); BSU (Biological study, unclassified); NUU (Other use, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process); USES (Uses)
(ionic and structural specificity effects of natural and synthetic polyamines on the aggregation and resolubilization of single-, double-, and triple-stranded DNA)

RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



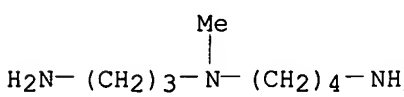
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:668497 CAPLUS
DOCUMENT NUMBER: 130:32686
TITLE: QSAR analysis of polyamine transport inhibitors in L1210 cells
AUTHOR(S): Xia, Cindy Q.; Yang, Johnny J.; Ren, Shijun; Lien, Eric J.
CORPORATE SOURCE: Department Pharmaceutical Sciences, School Pharmacy, University Southern California, Los Angeles, CA, 90033, USA
SOURCE: Journal of Drug Targeting (1998), 6(1), 65-77
CODEN: JDTAEH; ISSN: 1061-186X
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this paper, the authors attempt to construct a math. model to correlate the biol. activities of 63 polyamine transport inhibitors in L1210 cells with their physicochem. parameters. The inhibitory consts. (Ki) were obtained from the published work of Bergeron et al. Non-weighted least square method was used in deriving the regression equations with a BMDP program. An AM1 subroutine of the HyperChem program was used to optimize the geometry and calculate the mol. dipole moments and the distance between 2 terminal amino groups. A CQSAR program was used to calculate Clog P (oct./w.). A good correlation was obtained by a 5-parameter equation including the distance between 2 terminal amino groups (d), the number of cationic charge (Charge), mol. weight (MW), dipole moment (μ), and hydrogen bond forming ability (Hb). This model accounts for 81% of the variance in the data and can be used to estimate transport-inhibitory activity of many other polyamine analogs. It gives some quant. information about the relationship between the polyamine analogs function as transport inhibitors and their mol. structures.

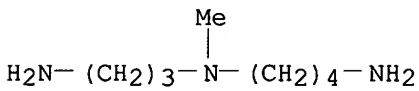
IT **51460-23-2**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(QSAR anal. of polyamine transport inhibitors in L1210 cells)

RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

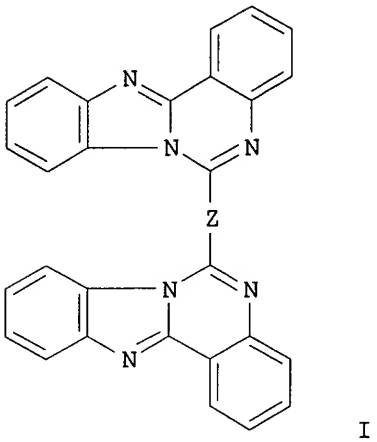
L4 ANSWER 29 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:801517 CAPLUS
DOCUMENT NUMBER: 128:152313
TITLE: Rapid induction of apoptosis by deregulated uptake of polyamine analogs
AUTHOR(S): Hu, Rei-Huang; Pegg, Anthony E.
CORPORATE SOURCE: Departments of Cellular and Molecular Physiology and Pharmacology, M. S. Hershey Medical Center, Pennsylvania State University College of Medicine, Hershey, PA, 17033, USA
SOURCE: Biochemical Journal (1997), 328(1), 307-316
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Treatment of Chinese hamster ovary cells with α-difluoromethylornithine for 3 days, followed by exposure to cycloheximide, led to an unregulated, rapid and massive accumulation of polyamine analogs. This accumulation led to cell death by apoptosis within a few hours. Clear evidence of DNA fragmentation was seen in response to both N-terminally ethylated polyamines and to polyamines containing Me groups on the terminal carbon atoms. Programmed cell death was induced within 2-4 h of exposure to 1 μM or higher concns. of N1,N11-bis(ethyl)norspermine. The presence of cycloheximide increased the uptake of the polyamine analogs and therefore led to cell death at lower analog concns., but it was not essential for the induction of apoptosis, since similar effects were seen when the protein synthesis inhibitor was omitted and the concentration of N1,N11-bis(ethyl)norspermine was increased to 5 μM or more The induction of apoptosis was blocked both by the addition of the caspase inhibitor N-benzyloxycarbonyl-Val-Ala-Asp-fluoromethylketone, or by the addition of the polyamine oxidase inhibitor N1-methyl-N2-(2,3-butadienyl)butane-1,4-diamine (MDL 72,527). These expts. provide evidence to support the concepts that: (1) polyamines or their oxidation products may be initiators of programmed cell death; (2) regulation of polyamine biosynthesis and uptake prevents the accumulation of toxic levels of polyamines; and (3) the antineoplastic effects of bis(ethyl) polyamine analogs may be due to the induction of apoptosis in sensitive tumor cells.
IT **51460-23-2**
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(rapid induction of apoptosis by deregulated uptake of polyamine analogs)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:458926 CAPLUS
DOCUMENT NUMBER: 127:190701
TITLE: Benzimidazo[1,2-c]quinazoline dimers as potential antitumor agents
AUTHOR(S): Brana, Miguel F.; De Vega, Maria Jesus Perez; Perron, Denise; Conlon, Donna; Bousquet, Peter F.; Robinson, Simon P.
CORPORATE SOURCE: Laboratorios Knoll S.A., Madrid, 28050, Spain
SOURCE: Journal of Heterocyclic Chemistry (1997), 34(3), 807-812

CODEN: JHTCAD; ISSN: 0022-152X
PUBLISHER: HeteroCorporation
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

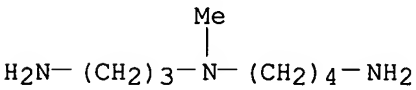


I

AB Title compds. I [Z = (CH2)3NMe(CH2)3, (CH2)3NH(CH2)4, (CH2)3NMe(CH2)4, (CH2)2NMe(CH2)2NMe(CH2)2, (CH2)2NMe(CH2)3NMe(CH2)2] were prepared from the mercaptobenzimidazoquinazoline and the diamines. I [Z = (CH2)3NMe(CH2)3] had a cytotoxic IC50 of 0.5 μM. When tested in vivo, however, no clear antitumor activity was produced in the human breast cancer tumor line MX-1 or the human melanoma tumor line LOX.

IT **51460-23-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of benzimidazo[1,2-c]quinazoline dimers as potential antitumor agents)

RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

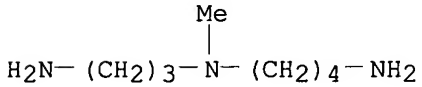
L4 ANSWER 31 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:71614 CAPLUS
DOCUMENT NUMBER: 126:166095
TITLE: Comparative molecular field analysis-based predictive model of structure-function relationships of polyamine transport inhibitors in L1210 cells
AUTHOR(S): Li, Yanlong; Mackerell, Alexander D., Jr.; Egorin, Merrill J.; Ballesteros, Michael F.; Rosen, D. Marc; Wu, Yi-Ying; Blamble, Deborah A.; Callery, Patrick S.
CORPORATE SOURCE: Department of Pharmaceutical Sciences, School of Pharmacy, University of Maryland, Baltimore, MD, 21201, USA
SOURCE: Cancer Research (1997), 57(2), 234-239
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Maintenance of intracellular polyamine concns. necessary for cell growth and proliferation is regulated in part by an energy-dependent polyamine

uptake system. To obtain information on the characteristics of the polyamine uptake system in L1210 leukemia cells, we have applied computational chemical techniques to the study of relationships between structure and function of 57 polyamine analogs. Ki values of polyamine analogs, derived from competitive inhibition of [3H]spermidine transport into L1210 cells, were chosen as the measure of biol. activity. Using comparative mol. field anal. (CoMFA), a model was constructed to relate mol. structure with biol. activity. The model was based on 4 monocationic, 8 dicationic, 14 tricationic, and 20 tetracationic polyamine analogs with a range of Ki values for the inhibition of [3H]spermidine uptake of 0.97-521 μM. The CoMFA model successfully predicted the inhibitory potency of 11 polyamines that had not previously been tested for polyamine uptake inhibitory activity. The 11 values predicted were within 33±62% of the actual Ki values. The test group included aziridinyl diamines, acetylated spermidines, two new oxazolidinonyl spermidines, monoaziridinyl spermidines, and a diaziridinyl spermine. Several of the compds. from this test group have been shown to have anticancer activity in mice. Consistent with the CoMFA model, certain basic functional groups, such as aziridines that have pKa values in the range of 6-7, seem to interact with the polyamine transporter in a cationic form. The results suggest that the CoMFA model is useful in drug design strategies as a predictive tool for the discovery of new anticancer agents that utilize a polyamine transporter for cellular uptake.

IT **51460-23-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CoMFA-based predictive model of structure-function relationships of polyamine transport inhibitors in L1210 cells)

RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 32 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:647095 CAPLUS
DOCUMENT NUMBER: 125:295391
TITLE: Structural specificity effects of trivalent polyamine analogs on the stabilization and conformational plasticity of triplex DNA
AUTHOR(S): Thomas, T. J.; Kulkarni, Gayathri D.; Greenfield, Norma J.; Shirahata, Akira; Thomas, Thresia
CORPORATE SOURCE: Dep. Med., Neurosci. Cell Biol., Univ. Med. and Dent. NJ-Robert Wood Johnson Med. Sch., New Brunswick, NJ, 08903, USA
SOURCE: Biochemical Journal (1996), 319(2), 591-599
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English

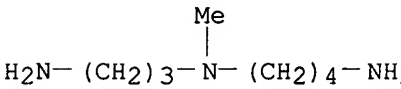
AB Natural polyamines, i.e. putrescine, spermidine and spermine, are excellent promoters of triplex DNA. Using melting temperature (Tm) measurements and CD spectroscopy, we found that structural alterations on the spermidine backbone, including methylation, or acetylation at the N1-, N4-, and/or N8-positions had a profound influence on the stability and conformation of poly(dA).2poly(dT) triplex. The conformation of the polynucleotide complex underwent sequential changes from B-DNA to triplex DNA as the concentration of spermidine increased from 0 to 50 μM in a buffer containing 10 mM sodium cacodylate and 1 mM EDTA (pH 7.2). At 60 μM spermidine, the CD spectrum of triplex DNA was comparable with that of ψ-DNA, with a strong pos. band centered around 260 nm. A neg. band was also found at 295 nm. At higher concns. of spermidine, however, the

intensity of the pos. band progressively decreased, and the peak intensity was found at a 1:0.3 molar ratio of DNA phosphate:spermidine. Temperature-dependent CD anal. showed that the ψ-DNA structure melted to single-stranded DNA at temps. above the Tm determined from the absorbance vs. temperature profile. Comparable effects were exerted on the conformation of triplex DNA by Co(NH3)63+, an inorg. trivalent cation. Substitution of the N4-hydrogen of spermidine by a cyclohexyl ring or the fusion of the N4-nitrogen in a cyclic ring system, as in piperidine, enhanced the ability of spermidine analogs to stabilize triplex and ψ-DNA forms over a wider concentration range compared with spermidine. These data demonstrate a differential effect of trivalent cations in stabilizing triplex DNA and provoking unusual conformation such as ψ-DNA. Synthetic homologues of spermidine that stabilize triplex DNA over a wider range of concns. than that stabilized by spermidine itself might have potential therapeutic applications in the development of an anti-gene strategy against several diseases, including cancer and AIDS.

IT **51460-23-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(structurally specific effects of trivalent polyamines on stabilization and conformational plasticity of triplex DNA)

RN 51460-23-2 CAPLUS

CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



L4 ANSWER 33 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:554182 CAPLUS

DOCUMENT NUMBER: 122:306683

TITLE: Search for novel ligands selective at a polyamine recognition domain on the N-methyl-D-aspartate receptor complex using membrane binding techniques

AUTHOR(S): Yoneda, Yukio; Ogita, Kiyokazu; Enomoto, Riyo; Kojima, Sumiko; Shuto, Makoto; Shirahata, Akira; Samejima, Keijiro

CORPORATE SOURCE: Department of Pharmacology, Faculty of Pharmaceutical Sciences, Setsunan University, 45-1 Nagaotoge-cho, Hirakata, Osaka, 573-01, Japan

SOURCE: Brain Research (1995), 679(1), 15-24
CODEN: BRREAP; ISSN: 0006-8993

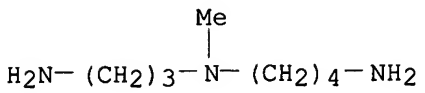
PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

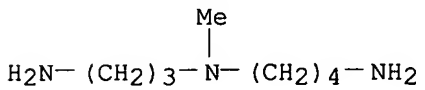
LANGUAGE: English

AB Among over 60 polyamine derivs. tested, only N-(3-aminopropyl)octanediamine and bis-(3-aminopropyl)nonanediamine (TE 393) markedly inhibited [3H](+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5,10-imine (MK-801) binding at equilibrium in the presence of added spermidine (SPD) in non-washed rat brain synaptic membranes, without affecting that in the absence of added SPD. Although TE 393 significantly potentiated [3H]MK-801 binding before equilibrium in the presence of L-glutamic acid (Glu) alone or both Glu and glycine (Gly) added in Triton-treated membranes, the putative polyamine antagonists 1,10-decanediamine (DA10) and arcaine invariably inhibited binding irresp. of the addition of agonists. In the absence of added SPD, in addition, TE 393 markedly enhanced abilities of both Glu and Gly to potentiate [3H]MK-801 binding before equilibrium However, TE 393 induced a rightward shift of the concentration-response curve of SPD for [3H]MK-801 binding before equilibrium Moreover, TE 393 was effective in potentiating binding of an antagonist but not an agonist radioligand to the NMDA domain and in inhibiting binding of an antagonist but not an agonist radioligand to the Gly domain. The potentiation of NMDA antagonist binding by TE 393 occurred in a manner sensitive to prevention by arcaine but not by DA10. TE 393 may be a novel ligand at the polyamine domain with an ability to interact with both the NMDA and Gly recognition domains in antagonist-preferring forms.

IT **51460-23-2**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(ligands selective at polyamine recognition domain on NMDA receptor complex)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



L4 ANSWER 34 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:96941 CAPLUS
DOCUMENT NUMBER: 120:96941
TITLE: The involvement of polyamines in the activation of vitamin D receptor from porcine intestinal mucosa
AUTHOR(S): Morishima, Yoshihiro; Inaba, Masaaki; Nishizawa, Yoshiki; Morii, Hirotoshi; Hasuma, Tadayoshi; Matsui-Yuasa, Isao; Otani, Shuzo
CORPORATE SOURCE: Med. Sch., Osaka City Univ., Japan
SOURCE: European Journal of Biochemistry (1994), 219(1-2), 349-56
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the intracellular process of the action of calcitriol, the vitamin D receptor is thought to undergo some kind of physicochem. change, called activation, before the receptor binds to the vitamin D response element of the gene. In this paper, the effects of polyamines and their analogs on the sedimentation properties of vitamin D receptor prepared from porcine intestinal mucosa, and on DNA binding activity of the receptor, were studied. In sucrose d. gradient anal., polyamines decreased the sedimentation coefficient of vitamin D receptor in a dose-dependent fashion. Polyamines increased DNA binding activity of vitamin D receptor dose-dependently. These findings show that polyamines can activate vitamin D receptor in vitro. Among naturally existing polyamines, spermidine and spermine, but not putrescine, were effective within their physiol. intracellular concns., suggesting that both spermidine and spermine can activate vitamin D receptor in vivo as well. Sucrose d. gradient anal. using various kinds of polyamine analogs having various nos. of cations showed that the number of cations of polyamines is important for the efficiency to change the sedimentation coefficient of vitamin D receptor, and that the distance between two cationic charges does not play an important role.
IT **51460-23-2**
RL: BIOL (Biological study)
(vitamin D receptor activation response to, in intestinal mucosa)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



L4 ANSWER 35 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:424371 CAPLUS
DOCUMENT NUMBER: 115:24371
TITLE: Preparation of acylpolyamines as plant growth regulators
INVENTOR(S): Brayer, Jean Louis; Martin, Claude; Mourioux, Gilles; Taliani, Laurent; Tessier, Jean
PATENT ASSIGNEE(S): Roussel-UCLAF, Fr.

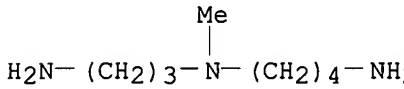
SOURCE: Fr. Demande, 36 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2644037	A1	19900914	FR 1989-3093	19890309
FR 2644037	B1	19911213		
WO 9010386	A1	19900920	WO 1990-FR163	19900309
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
EP 413807	A1	19910227	EP 1990-904860	19900309
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 03504511	T2	19911003	JP 1990-504948	19900309

PRIORITY APPLN. INFO.: FR 1989-3093 A 19890309
WO 1990-FR163 W 19900309
OTHER SOURCE(S): CASREACT 115:24371; MARPAT 115:24371

AB The acylpolyamines RCH2CONHWNHZ [R = aryl, heterocyclyl, aryloxy, etc.; W = (CH2)n, (CH2)mNY(CH2)o; Z = HC(:NH)NH2, C(:NCO2R1)NHCO2R1; Y = H, alkyl, aryl, etc.; R1 = alkyl, aralkyl, etc.; n, m, o = 2-6] are prepared as plant growth regulators. 4-Benzyloxy-3-methoxyphenoxyacetic acid was reacted with N-tert-butoxycarbonyl-1,4-diaminobutane in CH2Cl2, in the presence of dimethylaminopyridine and dicyclohexylcarbodiimide, to give N-[(4-benzyloxy-3-methoxyphenoxy)acetyl]-N1-(tert-butoxycarbonyl)-1,4-diaminobutane. This was reduced with Pd/C in EtOH-cyclohexane, to give N-[(4-hydroxy-3-methoxyphenoxy)acetyl]-N-(tert-butoxycarbonyl)-1,4-diamiobutane, which upon refluxing with HCl in EtOH gave N-[(4-hydroxy-3-methoxyphenoxy)acetyl]-1,4-diaminobutane (I). I (10-5-10-3 M) stimulated callus and root formation in tobacco leaf tissue culture.

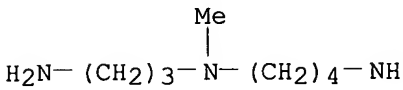
IT **51460-23-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with dichlorophenoxyacetic acid)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



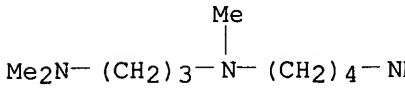
L4 ANSWER 36 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:121758 CAPLUS
DOCUMENT NUMBER: 114:121758
TITLE: Preparation of aryl- and aryloxyacetyldiaminoalkanes and analogs as agrochemical fungicides
INVENTOR(S): Brayer, Jean Louis; Taliani, Laurent; Tessier, Jean
PATENT ASSIGNEE(S): Roussel-UCLAF, Fr.
SOURCE: Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 376819	A1	19900704	EP 1989-403614	19891222
R: BE, CH, DE, ES, FR, GB, IT, LI, LU, NL				
FR 2642422	A1	19900803	FR 1988-16994	19881222
FR 2642422	B1	19940713		
US 5064861	A	19911112	US 1989-454685	19891221
JP 02225450	A2	19900907	JP 1989-331482	19891222

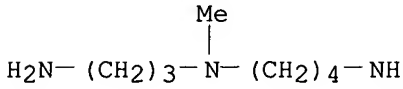
PRIORITY APPLN. INFO.: FR 1988-16994 A 19881222
OTHER SOURCE(S): CASREACT 114:121758; MARPAT 114:121758
AB R1CH2CONHWNHZ (I) [R1 = ArO, aryl, heterocyclyl, etc.; Ar = (substituted) aryl, heterocyclyl, etc.; W = (CH2)n, (CH2)mNY(CH2)a; n, m, a = 2-6; Y = H, alkyl, (substituted) aryl, etc.; Z = H, C(:NH)NH2, CO2R2, etc.; R2 = alkyl] were prepared Reaction of N-(tert-butoxycarbonyl)-1,4-diaminobutane with 3- trifluoromethylphenoxyacetyl chloride, followed by deprotection in EtOH containing HCl, gave I.HCl [R1 = 3-trifluoromethylphenoxy; W = (CH2)4; Z = H]. N-[6-(sec-Butyl)-2,4-dichlorophenoxy]acetyldiamino-1,5-pentane at 500 ppm gave 70% control of Botrytis cinerea.
IT **51460-23-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of agrochem. fungicide)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



L4 ANSWER 37 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:512331 CAPLUS
DOCUMENT NUMBER: 113:112331
TITLE: Growth inhibition of Botrytis cinerea by compounds interfering with polyamine metabolism
AUTHOR(S): Smith, Terence A.; Barker, Jacqueline H. A.; Jung, Michel
CORPORATE SOURCE: Res. Stn. Long Ashton, Bristol, BS18 9AF, UK
SOURCE: Journal of General Microbiology (1990), 136(6), 985-92
CODEN: JGMIAN; ISSN: 0022-1287
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several inhibitors of ornithine and arginine decarboxylases reduced growth of the fungus B. cinerea cultured on Czapek Dox agar. Of these, the most effective were difluoromethylornithine (DFMO), dehydromonofluoromethylornithine, difluoromethylarginine, and dehydromonofluoromethylarginine. The growth inhibition due to 1 mM DFMO could be partially reversed with 1 μM putrescine. Other compds. causing significant reversal of DFMO-mediated growth inhibition included diaminopentane (cadaverine), diaminoheptane, spermidine, 7,7-difluorospermidine, spermine, bis(2-aminoethyl)amine, 2-hydroxy-1,3-diaminopropane, monoacetylputrescine, butenediamine, and aminoguanidine. Some compds., which were relatively innocuous by themselves, increased growth inhibition due to DFMO. Notably effective compds. were methylacetylenic putrescine, aminooxyaminopropane, butynediamine, 2,2-difluoroputrescine, diacetylputrescine, methylglyoxal bis(guanylhydrazone), streptomycin, certain methylated amines, and cyclohexylamine and related compds. Growth inhibition due to a homologous series of diguanidines [NH2C(:NH)NH(CH2)xNHC(:NH)NH2] was also tested. These were especially effective when x = 12, and when x = 5 or 6. In general, the results suggest that amino acid-based inhibitors of ornithine decarboxylase have a greater permeability than amine-based inhibitors.
IT **54443-84-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(difluoromethylornithine inhibition of Botrytis cinerea response to)
RN 54443-84-4 CAPLUS
CN 1,4-Butanediamine, N-[3-(dimethylamino)propyl]-N,N',N'-trimethyl- (9CI) (CA INDEX NAME)

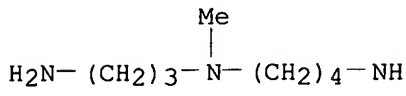


L4 ANSWER 38 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:550565 CAPLUS
DOCUMENT NUMBER: 105:150565
TITLE: Regulation of spermidine/spermine N1-acetyltransferase in L6 cells by polyamines and related compounds
AUTHOR(S): Erwin, Bradley G.; Pegg, Anthony E.
CORPORATE SOURCE: Coll. Med., Pennsylvania State Univ., Hershey, PA, 17033, USA
SOURCE: Biochemical Journal (1986), 238(2), 581-7
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Exposure of rat L6 cells in culture to exogenous polyamines led to a very large increase in the activity of spermidine/spermine N1-acetyltransferase (I). Spermine was more potent than spermidine (II) in bringing about this increase, but in both cases the elevated I activity increased the cellular conversion of II into putrescine. The I turned over very rapidly in the L6 cells, with a half-life of 9 min after II and 18 min after spermine. A wide variety of synthetic polyamine analogs also brought about a substantial induction of I activity. These included sym-norspermidine, sym-norspermine, sym-homospermidine, N4-substituted II derivs., 1,3,6-triaminohexane, 1,4,7-triaminoheptane, and deoxyspergualin, which were comparable with II in their potency, and N1,N8-bis(ethyl)spermidine, N1,N9-bis(ethyl)homospermidine, methylglyoxal bis(guanylhydrazone), ethylglyoxal bis(guanylhydrazone), and 1,1'-[(methylethanediylidene)dinitrilo]bis(3-aminoguanidine), which were even more active than II. These polyamine analogs may bring about a decrease in cellular polyamines not only by inhibiting biosynthesis but by stimulating the degradation of II into putrescine.
IT **51460-23-2**
RL: BIOL (Biological study)
(spermidine-spermine acetyltransferase of myoblasts response to)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)

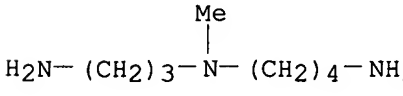


L4 ANSWER 39 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:125560 CAPLUS
DOCUMENT NUMBER: 104:125560
TITLE: The inhibition and activation of polyamine oxidase from oat seedlings
AUTHOR(S): Smith, Terence A.
CORPORATE SOURCE: Long Ashton Res. Stn., Univ. Bristol, Long Ashton/Bristol, BS18 9AF, UK
SOURCE: Plant Growth Regulation (1985), 3(3-4), 269-75
CODEN: PGRED3; ISSN: 0167-6903
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In a homologous series of diguanidines [NH2C(=NH)NH(CH2)xNHC(=NH)NH2] where x = 2-12, the greatest inhibition of polyamine oxidase of oat seedlings was found with x = 8. The synthetic fungicide guazatine was particularly effective as an inhibitor of polyamine oxidase, with a Ki of .apprx.10-8M. Inhibition due to the triamine derived from guazatine by hydrolysis was less effective by a factor of .apprx.200. Comparison of various inorg. salts at 1M showed that polyamine oxidase activity was enhanced in the order RbCl > KCl > KBr > NH4Cl > NaNO3 > LiCl = NaCl > control (no salt) > CaCl2 = MgCl2. Activity in RbCl was .apprx.4-5-fold greater than in the salt-free control. Enzyme activity is rapidly lost during assay. This loss of activity could not be attributed to inhibition by aminopropylpyrroline or diaminopropane. Moreover, the superoxide scavenger Cu salicylate did not protect enzyme activity.
IT **51460-23-2**

RL: BIOL (Biological study)
(polyamine oxidase of oat inhibition by, kinetics of)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)

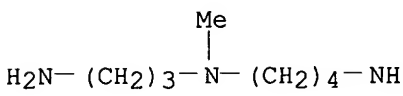


L4 ANSWER 40 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:431961 CAPLUS
DOCUMENT NUMBER: 103:31961
TITLE: Biological properties of N4- and N1,N8-spermidine derivatives in cultured L1210 leukemia cells
AUTHOR(S): Porter, Carl W.; Cavanaugh, Paul F., Jr.; Stolowich, Neal; Ganis, B.; Kelly, E.; Bergeron, Raymond J.
CORPORATE SOURCE: Grace Cancer Drug Cent., Roswell Park Mem. Inst., Buffalo, NY, 14263, USA
SOURCE: Cancer Research (1985), 45(5), 2050-7
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Eleven novel spermidine (I) [124-20-9] derivs. which are potential anticancer agents were evaluated for their ability to compete with 3H-labeled I for cellular uptake, to inhibit cell growth, to affect polyamine biosynthesis, to suppress enzyme activity, and to substitute for I in supporting growth of cultured L1210 leukemia cells. Uptake studies revealed N4-alkyl derivs. to be the most effective competitive inhibitors of [3H]I uptake followed by N1,N8-dialkyl derivs., then N4-acyl derivs., and N1,N8-diacyl derivs. The data indicate the relative importance of the terminal amines and of charge as determinants of cellular uptake. Of the 11 derivs., only N4-hexylspermidine [97141-39-4], N1,N8-diethylspermidine (II) [97141-40-7], and N1,N8-dipropylspermidine (III) [97141-41-8] demonstrated antiproliferative activity at 0.1 mM with 50%-inhibitory concentration values at 48 h of 30, 40, and 50 μM, resp. In the case of the N1,N8 I derivs., recovery from growth inhibition was enhanced considerably by exogenous I, suggesting involvement of polyamine depletion. At 10-30 μM, both II and III (but not N4-hexylspermidine) inhibited polyamine biosynthesis as indicated by redns. in polyamine pools and in biosynthetic enzyme activities. The more effective of the 2, II, depleted intracellular putrescine [110-60-1] and I and reduced spermine [71-44-3] by .apprx.50% at 96h and decreased ornithine decarboxylase [9024-60-6] and S-adenosylmethionine decarboxylase [9036-20-8] activities by 98 and 62%, resp. Since neither derivative (at 5 mM) directly inhibited these enzymes from untreated cell exts. by significantly more than I itself, they may act by regulating enzyme levels. None of the N4 I derivs. affected ornithine decarboxylase activity, whereas II and III were nearly as effective as I. Thus, the inhibition of cell growth via polyamine depletion occurs with those I derivs. (i.e. II or III) which regulate biosynthetic enzyme activities in a manner similar to polyamines but which, unlike the natural polyamines, are incapable of performing in functions essential for cell growth.
IT **51460-23-2**
RL: BIOL (Biological study)
(leukemia inhibition by, polyamine metabolism in relation to)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)

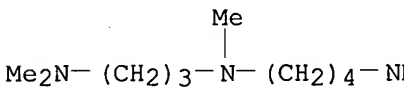


L4 ANSWER 41 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1985:95459 CAPLUS
DOCUMENT NUMBER: 102:95459
TITLE: Amines and polyamines from nitriles
AUTHOR(S): Bergeron, Raymond J.; Garlich, Joseph R.
CORPORATE SOURCE: Dep. Med. Chem., Univ. Florida, Gainesville, FL, 32610, USA
SOURCE: Synthesis (1984), (9), 782-4
CODEN: SYNTBF; ISSN: 0039-7881
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 102:95459
AB NC(CH2)nNR(CH2)mCN (R = H, CH2Ph, Me; m, n = 2,3), NCCH2CH2NH(CH2)4NHCH2CH2CN, and PhCH2NHCH2CH2CN were reduced by H in the presence of Raney Ni and NaOH to give H2N(CH2)n+1NR(CH2)m+1NH2. Debenzylation was avoided by the use of this catalyst.
IT **51460-23-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, by reduction of nitrile, catalysts for)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)

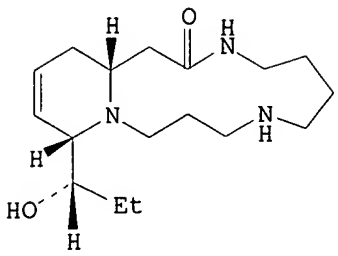


L4 ANSWER 42 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:134743 CAPLUS
DOCUMENT NUMBER: 90:134743
TITLE: A novel method of N-permethylation of amines and polyamines
AUTHOR(S): Chiavari, G.; Giumanini, A. G.; Rossi, P.
CORPORATE SOURCE: Ist. Chim. G. Ciamician, Univ. Bologna, Bologna, Italy
SOURCE: Italian Journal of Biochemistry (1978), 27(5), 336-8
CODEN: IJBIAC; ISSN: 0021-2938
DOCUMENT TYPE: Journal
LANGUAGE: English
AB NaBH4 in acidic aqueous solution was used to produce N-permethylated amines. The reaction was used on aliphatic and polyamines of biol. interest; yields were 80-100%. Aromatic amines were N-permethylated by using NaBH4 in EtOH-tetrahydrofurane in acidic-H2CO-H2O solution These derivs. may then be used for gas chromatog.-mass spectrometry.
IT **54443-84-4**
RL: PRP (Properties)
(mass spectrum of)
RN 54443-84-4 CAPLUS
CN 1,4-Butanediamine, N-[3-(dimethylamino)propyl]-N,N',N'-trimethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 43 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:529769 CAPLUS
DOCUMENT NUMBER: 89:129769
TITLE: Horsetail alkaloids. Part 15. Degradation of palustrine to (-)-dihydropalustramic acid ((2R,6S,1'S)-[6-(1'-hydroxypropyl)-2-piperidyl]acetic acid), and the structure of palustrine and palustridine
AUTHOR(S): Mayer, Carl; Green, Clinton Ludlow; Trueb, Werner; Waelchli, Peter Christian; Eugster, Conrad Hans
CORPORATE SOURCE: Org.-Chem. Inst., Univ. Zurich, Zurich, Switz.

SOURCE: Helvetica Chimica Acta (1978), 61(2), 905-21
CODEN: HCACAV; ISSN: 0018-019X
DOCUMENT TYPE: Journal
LANGUAGE: German
GI



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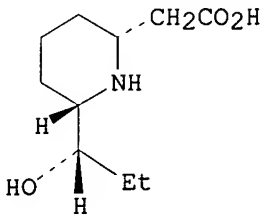
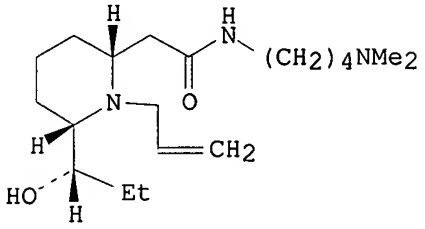
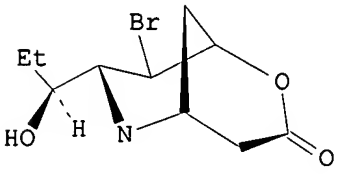


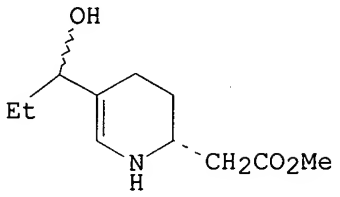
II



III



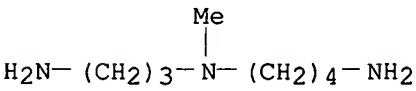
IV



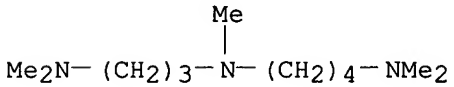
V

AB The structure of the macrocyclic alkaloid palustrine is shown to be I. Its piperidine unit can be obtained as (-)-dihydropalustramic acid (II) by the following sequence of degradation reactions: catalytic hydrogenation of I followed by methylation and Hofmann degradation provides the allyl base III. Catalytic reduction of III and subsequent acidic hydrolysis yielded II and N,N-dimethylputrescine. Loss of the N-alkyl group in the formation of II occurs during the catalytic hydrogenation step. This interpretation is supported by the results of model expts. The position of the double bond in I is deduced from the IR spectrum of the bromo-δ-lactone IV prepared by treatment of I with N-bromosuccinimide at pH 4. Some of the authors' previously published results on the degradation of dihydropalustrine are obviously at variance with the newly proposed structure for palustrine. They can easily be explained by assuming a partial hydrogenolysis of the C(17)-N(1) bond during the preparation of dihydropalustrin from palustrine. Periodate cleavage of dihydropalustramine acid Me ester liberates propionaldehyde, at lower pH values it condensates rapidly with the simultaneously generated 3,4,5,6-tetrahydropyridine derivative The structure of the condensation product is proposed to be V on the basis of the isolation of its hydrogenation product, an isomeric dihydropalustramic acid.

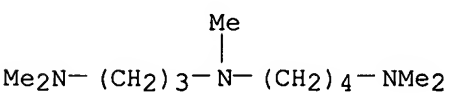
IT **51460-23-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 51460-23-2 CAPLUS
CN 1,4-Butanediamine, N-(3-aminopropyl)-N-methyl- (9CI) (CA INDEX NAME)



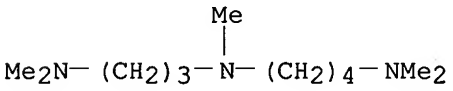
L4 ANSWER 44 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1977:464835 CAPLUS
DOCUMENT NUMBER: 87:64835
TITLE: A new method of derivatization of amines and polyamines for gas chromatography and mass spectrometry
AUTHOR(S): Giumanini, Angelo G.; Chiavari, Giuseppe
CORPORATE SOURCE: Ist. G. Ciamician, Univ. Bologna, Bologna, Italy
SOURCE: Appl. Spectrom. Masse (SM) Reson. Magn. Nucl. (RMN) Ind. Aliment., [Symp. Int. Comm. Int. Ind. Agric. Aliment.], 15th (1977), Meeting Date 1975, 423-6. Comm. Int. Ind. Agric. Aliment.: Paris, Fr.
CODEN: 35TFAI
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Solid NaBH4 was added to an acidic solution of polyamines (α,ω-diamines, spermidine, and spermine) and H2CO at 0 to -20° to yield single N-permethylated polyamines. The derivatization yield was 70% for ethylenediamine to >90% for spermidine. The N-permethylated polyamines (C2-C8) were separated on a 1 m + 2.5 mm Chromosorb P-Carbowax 20 M 5%-KOH 5% column, programmed temperature 80-170° at 3°/min, flow rate 15 mL/min. Mass spectra of spermine and spermidine are presented. The method is easy and inexpensive.
IT **54443-84-4P**
RL: PREP (Preparation)
(preparation and mass spectra)
RN 54443-84-4 CAPLUS
CN 1,4-Butanediamine, N-[3-(dimethylamino)propyl]-N,N',N'-trimethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 45 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:4389 CAPLUS
DOCUMENT NUMBER: 84:4389
TITLE: Facile synthesis of N-permethylspermine and N-permethylspermidine from their unmethylated precursors
AUTHOR(S): Giumanini, Angelo G.; Chiavari, Giuseppe; Scarponi, Franco L.
CORPORATE SOURCE: Ist. Chim. G. Ciamician, Univ. Bologna, Bologna, Italy
SOURCE: Zeitschrift fuer Naturforschung, Teil B: Anorganische Chemie, Organische Chemie (1975), 30B(9-10), 820-1
CODEN: ZNBAD2; ISSN: 0340-5087
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A rapid synthesis of the title compds. employing H2CO and NaBH4 in acidic aqueous solution in combination with the unmethylated amines is described. High yields and the characteristics of the methylated amines allow the application of the method to gas chromatog. and mass spectrometric analyses.
IT **54443-84-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and gas chromatog.-mass spectra of)
RN 54443-84-4 CAPLUS
CN 1,4-Butanediamine, N-[3-(dimethylamino)propyl]-N,N',N'-trimethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 46 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1975:82097 CAPLUS
DOCUMENT NUMBER: 82:82097
TITLE: Further properties of the polyamine oxidase of barley leaves
AUTHOR(S): Smith, Terence A.; Bickley, Daisy A.
CORPORATE SOURCE: Long Ashton Res. Stn., Long Ashton/Bristol, UK
SOURCE: Phytochemistry (Elsevier) (1974), 13(11), 2437-43
CODEN: PYTCAS; ISSN: 0031-9422
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Polyamine analogs were studied as potential inhibitors or substrates of barley leaf polyamine oxidase. NH2(CH2)3NH(CH2)10NH2 was particularly effective as an inhibitor of spermine oxidation at pH 4.5 (Ki = 5 + 10-6 M). Methylglyoxal-bis(guanylhydrazone) inhibited spermine oxidation only slightly (Ki = 10-4 M). Activity with the polyamine analogs as substrates was generally 10% or less of the activity with spermine. The Km for O was 3 + 10-4 M. The Km for spermine oxidation was independent of O concentration Using the N-methyl-2-benzothiazolone hydrazine reagent, 1-(3-aminopropyl)pyrroline was shown to be formed stoichiometrically by the enzyme on oxidation of spermine. The enzyme will not function as a dehydrogenase in the presence of O with either K ferricyanide or dichlorophenolindophenol as electron acceptors. Activity in the leaves increased with age, up to 4 weeks. In the leaves of 11-week-old plants activity was lower than in leaves of 1-week-old plants. The enzyme was mainly associated with an easily-sedimented particulate fraction, and relatively small proportions were found in the cell wall or soluble fractions.
IT **54443-84-4**
RL: BIOL (Biological study)
(polyamine oxidase inhibition by, kinetics of)
RN 54443-84-4 CAPLUS
CN 1,4-Butanediamine, N-[3-(dimethylamino)propyl]-N,N',N'-trimethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 47 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:163695 CAPLUS
DOCUMENT NUMBER: 144:384807
TITLE: Guide Molecule-driven Stereospecific Degradation of α-Methylpolyamines by Polyamine Oxidase
AUTHOR(S): Jaervinen, Aki; Keinaenen, Tuomo A.; Grigorenko, Nikolay A.; Khomutov, Alex R.; Uimari, Anne; Vepsaelaeinen, Jouko; Naervaenen, Ale; Alhonen, Leena; Jaenne, Juhani
CORPORATE SOURCE: A. I. Virtanen Institute for Molecular Sciences and the Department of Chemistry, University of Kuopio, Kuopio, FI-70211, Finland
SOURCE: Journal of Biological Chemistry (2006), 281(8), 4589-4595
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB FAD-dependent polyamine oxidase (PAO; EC 1.5.3.11) is one of the key enzymes in the catabolism of polyamines spermidine and spermine. The natural substrates for the enzyme are N1-acetylspermidine, N1-acetylspermine, and N1,N12-diacetylspermine. Here we report that PAO, which normally metabolizes achiral substrates, oxidized (R)-isomer of 1-amino-8-acetamido-5-azanonane and N1-acetylspermidine as efficiently while (S)-1-amino-8-acetamido-5-azanonane was a much less preferred

substrate. It has been shown that in the presence of certain aldehydes, the substrate specificity of PAO and the kinetics of the reaction are changed to favor spermine and spermidine as substrates. Therefore, we examined the effect of several aldehydes on the ability of PAO to oxidize different enantiomers of α-methylated polyamines. PAO supplemented with benzaldehyde predominantly catalyzed the cleavage of (R)-isomer of α- **methylspermidine**, whereas in the presence of pyridoxal the (S)-α- **methylspermidine** was preferred. PAO displayed the same stereospecificity with both singly and doubly α-methylated spermine derivs. when supplemented with the same aldehydes. Structurally related ketones proved to be ineffective. This is the first time that the stereospecificity of FAD-dependent oxidase has been successfully regulated by changing the supplementary aldehyde. These findings might facilitate the chemical regulation of stereospecificity of the enzymes.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 48 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:106729 CAPLUS

TITLE: Activated polyamine catabolism in acute pancreatitis: α-methylated polyamine analogues prevent trypsinogen activation and pancreatitis-associated mortality

AUTHOR(S): Hyvonen, Mervi T.; Herzig, Karl-Heinz; Sinervirta, Riitta; Albrecht, Elke; Nordback, Isto; Sand, Juhani; Keinanen, Tuomo A.; Vepsalainen, Jouko; Grigorenko, Nikolay; Khomutov, Alex R.; Kruger, Burkhard; Janne, Juhani; Alhonen, Leena

CORPORATE SOURCE: Department of Biotechnology and Molecular Medicine, A. I. Virtanen Institute for Molecular Sciences, University of Kuopio, Kuopio, Finland

SOURCE: American Journal of Pathology (2005), Volume Date 2006, 168(1), 115-122
CODEN: AJPAA4; ISSN: 0002-9440

PUBLISHER: American Society for Investigative Pathology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Polyamines are essential for normal cellular growth and function. Activation of polyamine catabolism in transgenic rats overexpressing spermidine/spermine N1-acetyltransferase, the key enzyme in polyamine catabolism, results in severe acute pancreatitis. Here, we investigated the role of polyamine catabolism in pancreatitis and studied the effect of polyamine analogs on the outcome of the disease. Polyamine depletion was associated with arginine- and caerulein-induced pancreatitis as well as with human acute necrotizing and chronic secondary pancreatitis. Substitution of depleted polyamine pools with **methylspermidine** partially prevented arginine-induced necrotizing pancreatitis whereas caerulein-induced edematous pancreatitis remained unaffected. Transgenic rats receiving methylated polyamine analogs after the induction of pancreatitis showed less pancreatic damage than the untreated rats. Most importantly, polyamine analogs dramatically rescued the animals from pancreatitis-associated mortality. Induction of spermidine/spermine N1-acetyltransferase in acinar cells isolated from transgenic rats resulted in increased trypsinogen activation. Pretreatment of acini with bismethylspermine prevented trypsinogen activation, indicating that premature proteolytic activation is one of the effects triggered by polyamine depletion. Our data suggest that activation of polyamine catabolism is a general pathway in the pathogenesis of acute pancreatitis and that exptl. disease can be ameliorated with stable polyamine analogs.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 49 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1306975 CAPLUS

DOCUMENT NUMBER: 144:212934

TITLE: α-Methyl Polyamines: Efficient Synthesis and Tolerance Studies in Vivo and in Vitro. First Evidence for Dormant Stereospecificity of Polyamine Oxidase

AUTHOR(S): Jaervinen, Aki J.; Cerrada-Gimenez, Marc; Grigorenko,

Nikolay A.; Khomutov, Alex R.; Vepsaelaeinen, Jouko J.; Sinervirta, Riitta M.; Keinaenen, Tuomo A.; Alhonen, Leena I.; Jaenne, Juhani E.

CORPORATE SOURCE: Department of Biotechnology and Molecular Medicine, A.I. Virtanen Institute for Molecular Sciences, and Department of Chemistry, University of Kuopio, Kuopio, Finland

SOURCE: Journal of Medicinal Chemistry (2006), 49(1), 399-406
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:212934

AB Efficient syntheses of metabolically stable α-**methylspermidine**, α-methylspermine, and bis-α,α'-methylated spermine starting from Et 3-aminobutyrate are described. The biol. tolerance for these compds. was tested in wild-type mice and transgenic mice carrying the metallothionein promoter-driven spermidine/spermine N1-acetyltransferase gene (MT-SSAT). The efficient substitution of natural polyamines by their derivs. was confirmed in vivo with the rats harboring the same MT-SSAT transgene and in vitro with the immortalized fibroblasts derived from these animals. Enantiomers of previously unknown 1-amino-8-acetamido-5-azanonane dihydrochloride (I) were synthesized starting from enantiomerically pure (R)- and (S)-alaninols. The studies with recombinant human polyamine oxidase (PAO) showed that PAO (usually splits achiral substrates) strongly favors the (R)-isomer of I that demonstrates for the first time that the enzyme has hidden potency for stereospecificity.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 50 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:621292 CAPLUS
DOCUMENT NUMBER: 121:221292

TITLE: Effects of the S-adenosylmethionine decarboxylase inhibitor, 5'-{[(Z)-4-amino-2-butenyl]methylamino}-5'-deoxyadenosine, on cell growth and polyamine metabolism and transport in Chinese hamster ovary cell cultures

AUTHOR(S): Byers, Timothy L.; Wechter, Rita S.; Hu, Rei-Huang; Pegg, Anthony E.

CORPORATE SOURCE: Coll. Med., Pennsylvania State Univ., Hershey, PA, 17033, USA

SOURCE: Biochemical Journal (1994), 303(1), 89-96
CODEN: BIJOAK; ISSN: 0264-6021
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The regulation of polyamine transport and the roles of polyamine transport and synthesis in cell growth were investigated using cultured Chinese hamster ovary (CHO) cells and CHOMG cells which are mutants lacking polyamine-transport activity. Metabolically stable methylated polyamine analogs were used to measure polyamine accumulation, and the irreversible S-adenosyl-L-methionine decarboxylase inhibitor, 5'-{[(Z)-4-amino-2-butenyl]methylamino}-5'-deoxyadenosine (AbeAdo), was used to inhibit synthesis. Exposure to AbeAdo led to a dose-dependent decrease in growth for both cell lines, although CHOMG cells were more sensitive. Intracellular putrescine levels were greatly increased in AbeAdo-treated CHO cells and to a lesser extent in CHOMG cells, whereas intracellular spermidine and spermine levels were substantially reduced in both. Treatment with AbeAdo increased putrescine content in the culture medium to a much greater extent in CHOMG cultures indicating that a portion of the excess putrescine synthesized in response to AbeAdo treatment is excreted, but that CHO cells salvage this putrescine whereas it is lost to CHOMG cells which cannot take up polyamines. AbeAdo treatment increased polyamine transport into CHO cells despite high intracellular putrescine, suggesting that spermidine and/or spermine, and not putrescine, are the major factors regulating transport activity. The accumulation of either 1-**methylspermidine** or 1,12-dimethylspermine was significantly increased by AbeAdo treatment. Accumulation was increased even further

when protein synthesis was blocked by cycloheximide, indicating that a short-lived protein is involved in the regulation of polyamine uptake. In the presence of cycloheximide and AbeAdo or α-difluoromethylornithine, methylated polyamine derivs. accumulated to very high levels leading to cell death. These results show that the polyamine-transport system plays an important role in retaining intracellular polyamines and that down-regulation of the transport system in response to increase intracellular polyamine content is necessary to prevent accumulation of toxic levels of polyamines.

L4 ANSWER 51 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:188652 CAPLUS
DOCUMENT NUMBER: 118:188652
TITLE: Enhancement of the spermidine uptake system and lethal effects of spermidine overaccumulation in ornithine decarboxylase-overproducing L1210 cells under hyposmotic stress
AUTHOR(S): Poulin, Richard; Coward, James K.; Lakanen, John R.; Pegg, Anthony E.
CORPORATE SOURCE: Coll. Med., Pennsylvania State Univ., Hershey, PA, 17033, USA
SOURCE: Journal of Biological Chemistry (1993), 268(7), 4690-8
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The D-R cell subline, an ornithine decarboxylase-overproducing variant of L1210 mouse leukemia cells, shows a growth advantage at low osmolality due to its high putrescine content. The ability of spermidine to fulfill the role of putrescine under hyposmotic conditions was tested. Although spermidine (1-30 μM) had no effect on growth under normosmotic conditions (325 mosm/kg), it was strongly inhibitory to D-R cell proliferation at 150 mosmol/kg in a concentration-dependent manner. Hypotonic shock greatly increased the rate of spermidine uptake in D-R cells. The increased spermidine content enhanced total putrescine synthesis through a large induction of cytosolic spermidine/spermine N1-acetyltransferase activity but also promoted the excretion of most of the putrescine synthesized by the cells. Delaying the addition of spermidine until 24 h after hypotonic shock resulted in a much sharper decrease in D-R cell viability and strongly depressed polyamine contents. These lethal effects occurred between 8 and 24 h after spermidine addition and followed a dramatic increase in the rate and extent of spermidine accumulation which overrode the metabolic capacity of the N1-acetyltransferase/polyamine oxidase (PAO) pathway. Inhibition of PAO partly reversed the effect of spermidine on growth when the polyamine was added at the time of hypotonic shock, but not 24 h later. Similar expts. performed with α-**methylspermidine**, a metabolically resistant analog, which can completely fulfill cellular requirements for spermidine in normosmotic media, suggested that the lethal effect of a delayed spermidine addition is caused predominantly by excessive accumulation with a minor contribution resulting from stress due to polyamine oxidase activity. In contrast, in hypotonically shocked L1210 cells, spermidine stimulated cell proliferation (albeit less effectively than putrescine), there was no lethal effect of a delayed addition of α- **methylspermidine**, and there was no time-dependent increase in the rate of α-**methylspermidine** uptake. Thus, the spermidine transport system is strongly enhanced by hyposmotic shock in D-R cells, which can result in extensive cell death from overaccumulation of the polyamine and, to a lesser extent, from stress related to the PAO-catalyzed degradation of N1-acetylspermidine. The absence of these effects in parental L1210 cells indicates that the acquisition of an ornithine decarboxylase-overproducing phenotype also involves major modifications in the expression and/or regulation of polyamine transport.

L4 ANSWER 52 OF 61 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:190838 BIOSIS
DOCUMENT NUMBER: PREV200600180634
TITLE: Activated polyamine catabolism in acute pancreatitis - alpha-methylated polyamine analogues prevent trypsinogen

activation and pancreatitis-associated mortality.
AUTHOR(S): Hyvonen, Mervi T.; Herzig, Karl-Heinz; Sinervirta, Riitta; Albrecht, Elke; Nordback, Isto; Sand, Juhani; Keinanen, Tuomo A.; Vepsalainen, Jouko; Grigorenko, Nikolay; Khomutov, Alex R.; Krueger, Burkhard; Jaenne, Juhani; Alhonen, Leena [Reprint Author]
CORPORATE SOURCE: Univ Kuopio, AI Virtanen Inst Mol Sci, Dept Biotechnol and Mol Med, POB 1627, FI-70211 Kuopio, Finland
leena.alhonen@uku.fi
SOURCE: American Journal of Pathology, (JAN 2006) Vol. 168, No. 1, pp. 115-122.
CODEN: AJPAA4. ISSN: 0002-9440.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Mar 2006
Last Updated on STN: 15 Mar 2006

AB Polyamines are essential for normal cellular growth and function. Activation of polyamine catabolism in transgenic rats overexpressing spermidine/spermine N-1-acetyltransferase, the key enzyme in polyamine catabolism, results in severe acute pancreatitis. Here, we investigated the role of polyamine catabolism in pancreatitis and studied the effect of polyamine analogues on the outcome of the disease. Polyamine depletion was associated with arginine- and cerulein-induced pancreatitis as well as with human acute necrotizing and chronic secondary pancreatitis. Substitution of depleted polyamine pools with **methylspermidine** partially prevented arginine-induced necrotizing pancreatitis whereas cerulein-induced edematous pancreatitis remained unaffected. Transgenic rats receiving methylated potyamine analogues after the induction of pancreatitis showed less pancreatic damage than the untreated rats. Most importantly, polyamine analogues dramatically rescued the animals from pancreatitis-associated mortality. Induction of spermidine/spermine N-1-acetyltransferase in acinar cells isolated from transgenic rats resulted in increased trypsinogen activation. Pretreatment of acini with bismediylspermine prevented trypsinogen activation, indicating that premature proteolytic activation is one of the effects triggered by polyamine depletion. Our data suggest that activation of polyamine catabolism is a general pathway in the pathogenesis of acute pancreatitis and that experimental disease can be ameliorated with stable polyamine analogues.

L4 ANSWER 53 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:170057 CAPLUS
DOCUMENT NUMBER: 126:223676
TITLE: Accumulation of hydroxyspermidine in red blood cells, a potential index of tumor proliferation rate
AUTHOR(S): Leveque, Jean; Delcros, Jean-Guy; Havouis, Rene; Quemener, Veronique; Vaultier, Michel; Seiler, Nikolaus; Moulinoux, Jacques-Philippe
CORPORATE SOURCE: Fac. Medecine, Univ. Rennes I, Rennes, 35043, Fr.
SOURCE: Anticancer Research (1996), 16(6B), 3745-3747
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has previously been demonstrated that during Lewis Lung carcinoma growth, red blood cell spermidine levels increase concomitantly with tumor volume If [14C] putrescine or 2-methylputrescine are administered, [14C] spermidine and **methylspermidine**, resp., accumulate in red blood cells in proportion with the tumor volume In the present work the metabolic transformation of 2-hydroxyputrescine, a natural derivative of putrescine, to hydroxyspermidine, was studied in tumor bearing mice. After a single i.p. injection of 2-hydroxyputrescine, higher concns. of hydroxyspermidine were found in the tumor than in liver. In the red blood cells of Lewis lung carcinoma-bearing mice, hydroxyspermidine was detected between 24 h and 96 h after i.p. injection of 2-hydroxyputrescine. The concentration of hydroxyspermidine found in red blood cells was proportional to the tumor volume Hydroxyspermidine has potential as a marker of malignant cell proliferation in human oncol.

L4 ANSWER 54 OF 61 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:209169 BIOSIS
DOCUMENT NUMBER: PREV200600210898
TITLE: Activated polyamine catabolism in acute experimental pancreatitis: Polyamine analogues as potential drugs to improve survival.
AUTHOR(S): Hyvonen, Mervi; Herzig, Karl-Heinz; Smervirta, Rinta; Albrecht, Elke; Nordback, Isto; Sand, Juhani; Keinanen, Tuomo A.; Vepsalainen, Jouko; Grigorenko, Nikolay; Khomutov, Alex R.; Kruger, Burkhard; Janne, Juhani; Alhonen, Leena
SOURCE: Gastroenterology, (APR 2005) Vol. 128, No. 4, Suppl. 2, pp. A378-A379.
Meeting Info.: Annual Meeting of the American-Gastroenterological-Association/Digestive-Disease-Week. Chicago, IL, USA. May 14 -19, 2005. Amer Gastroenterol Assoc.
CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Mar 2006
Last Updated on STN: 29 Mar 2006

AB Background: Polyamines are required for optimal growth and function of cells. Regulation of their cellular homeostasis is therefore tightly controlled. The key regulatory enzyme for polyamine catabolism is the spermidine/spermine N1-acetyltransferase (SSAT). Depletion of cellular polyamines has been associated with inhibition of growth and programmed cell death. Activation of polyamine catabolism in transgenic rats overexpressing SSAT induces severe acute pancreatitis. In this study we investigated the role of polyamine catabolism in different models of experimental pancreatitis and the effect of polyamine analogues on the pathophysiological mechanism and mortality of acute pancreatitis. Methods: Acute pancreatitis was induced in normal rats with L-arginine or cerulein with or without prior treatment with **methylspermidine** (MS). In transgenic rats overexpressing the SSAT gene under control of the inducible mouse metallothionein 1 Promoter, acute pancreatis was induced with zinc followed by administration of MS or bismethylspermine (BMS) at different times. Surgical resected pancreatic samples were obtained during operation from patients with acute or chronic pancreatitis. Pancreatic acini from wildtype and transgenic rats were prepared and intracellular trypsinogen activation was measured using a fluorescent probe. Results: In arginine or cerulein-induced pancreatitis pancreatic polyamine spermidine and spermine pools were significantly decreased. Pretreatment with MS alleviated pancreatitis caused by arginine but failed to prevent it totally. Cerulein-induced pancreatitis remained unaffected by MS. Transgenic rats receiving polyamine analogues after SSAT induction showed milder macroscopic and microscopic changes than the untreated rats. More importantly, polyamine analogues dramatically improved the long-term survival of the animals. Analysis of the human samples revealed that pancreatic polyamines were totally depleted in acute and decreased in chronic pancreatitis. Furthermore, BMS prevented trypsinogen activation in isolated acini from transgenic rats. Conclusions: Our results suggest that depletion of polyamines is a general trigger contributing to the development of pancreatitis. The outcome of the disease can be improved with polyamine analogues that fulfill the physiological requirements of the natural polyamines. Such polyamine analogues may prove useful in the therapy of human pancreatitis.

L4 ANSWER 55 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:195392 CAPLUS
DOCUMENT NUMBER: 143:303698
TITLE: Acute pancreatitis induced by activation of the polyamine catabolism in gene-modified mice and rats overexpressing spermidine/spermine N1-acetyltransferase
AUTHOR(S): Herzig, Karl-Heinz; Janne, Juhani; Alhonen, Leena
CORPORATE SOURCE: Department of Biotechnology and Molecular Medicine,

A.I. Virtanen Institute for Molecular Sciences, University of Kuopio, Finland
SOURCE: Scandinavian Journal of Gastroenterology (2005), 40(1), 120-121
CODEN: SJGRA4; ISSN: 0036-5521
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Premature intracellular activation of digestive zymogens is the initiating factor in the course of acute pancreatitis. In transgenic rats overexpressing spermidine/spermine N1-acetyltransferase (SSAT) gene under the control of an inducible mouse metallothionein I promoter, administration of zinc resulted in acute pancreatitis by depletion of spermidine and spermine. A sufficient pool of higher polyamine levels seems therefore essential to maintain pancreatic integrity. The induction of pancreatitis by activation of SSAT could be prevented by the administration of 1-**methylspermidine**, a metabolically stable analog of spermidine.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 56 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:552063 CAPLUS
DOCUMENT NUMBER: 141:82364
TITLE: Spermidine analogs for prevention and treatment of pancreatitis and induction of liver regeneration
INVENTOR(S): Rasanen, Tiina-Liisa; Alhonen, Leena; Sinervirta, Riitta; Keinanen, Tuomo; Herzig, Karl-Heinz; Khomutov, Alex Radii; Vepsalainen, Jouko; Janne, Juhani
PATENT ASSIGNEE(S): Tiina-Liisa Rasanen, Finland; Leena Alhonen; Riitta Sinervirta; Tuomo Keinanen; Karl-Heinz Herzig; Alex Radii Khomutov; Jouko Vepsalainen; Juhani Janne
SOURCE: Jpn. Kokai Tokkyo Koho, 51 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 2004189714	A2	20040708	JP 2003-33882		20030212
CA 2413720	AA	20040609	CA 2002-2413720		20021209
CA 2452467	AA	20040609	CA 2003-2452467		20031209
US 2004180968	A1	20040916	US 2003-731626		20031209
PRIORITY APPLN. INFO.:			US 2002-431958P	P	20021209
			CA 2002-2413720	A	20021209

OTHER SOURCE(S): MARPAT 141:82364
AB Spermidine analogs (I; R2R1N(CR3R4)aN(R10)(CR5R6)bN(R11)[(CR7R8)cN(R12)]nR 9 wherein a, b, c = 1-6; n = 0, 1; R1-R12 = H, alkyl), including 1-**methylspermidine**, are claimed for prevention and treatment of pancreatitis and induction of liver regeneration.

L4 ANSWER 57 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:174433 CAPLUS
DOCUMENT NUMBER: 124:283441
TITLE: An NMR self-diffusion study of the interactions between spermidine and oligonucleotides
AUTHOR(S): Andreasson, Bo; Nordenskioeld, Lars; Braunlin, William
CORPORATE SOURCE: Division Physical Chemistry, Stockholm Univ., Stockholm, S-106 91, Swed.
SOURCE: Biopolymers (1996), 38(4), 505-13
CODEN: BIPMAA; ISSN: 0006-3525
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Self-diffusion coeffs. have been determined by pulsed field gradient NMR methods for spermidine in solns. of the oligonucleotides d(GC)4 and d(GGAATTCC). The self-diffusion behavior of spermidine in solution of d(GC)4

is very similar to that observed previously for **methylspermidine** (completely N-methylated spermidine). Moreover, the self-diffusion behaviors of spermidine in solns. of d(GC)4 and d(GGAATTCC) are also quite similar, indicating that there is no significant influence on on self-diffusion of oligonucleotide base composition Furthermore, self-diffusion coeffs. of the oligonucleotide d(GC)8 show only a small dependence on oligonucleotide concentration, and no measurable dependence on sodium ion or magnesium ion concentration

L4 ANSWER 58 OF 61 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:3494 CAPLUS
DOCUMENT NUMBER: 118:3494
TITLE: Taxonomic significance of polyamine synthesis in Paracoccus
AUTHOR(S): Hamana, Koei; Matsuzaki, Shigeru
CORPORATE SOURCE: Coll. Med. Care Technol., Gunma Univ., Maebashi, 371, Japan
SOURCE: Journal of General and Applied Microbiology (1992), 38(2), 93-103
CODEN: JGAMA9; ISSN: 0022-1260
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Five Paracoccus spp., P. denitrificans, P. alcaliphilus, P. aminophilus, P. aminovorans, and P. kocurii, ubiquitously contained putrescine and spermidine as major polyamines. Spermine and cadaverine were detected sporadically in some strains as a minor component. All the strains of these species produced norspermidine from diaminopropane supplemented into the medium and some strains produced 2 aminopropyl derivs. of cadaverine, i.e., aminopropylcadaverine and aminopentylnorspermidine. The biosynthetic ability of these unusual polyamines serves as a chemotaxonomic marker in the genus Paracoccus. P. denitrificans IFO 13301 decarboxylated ε-N-methyllysine as well as lysine, but neither ε-N-acetyllysine nor δ-hydroxyllysine. The organism formed 2-hydroxyspermidine from the supplemented 2-hydroxyputrescine as well as 2-hydroxynorspermidine from 2-hydroxydiaminopropane, but not N-acetylspermidine and N-**methylspermidine** from N-acetylputrescine and N-methylputrescine, resp. A halophilic sp., P. halodentrificans, which contains spermidine as the major polyamine and has no norspermidine- and aminopropylcadaverine-synthetic potential, was suggested not to be a valid member of the genus Paracoccus.

L4 ANSWER 59 OF 61 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004111966 EMBASE
TITLE: Genetic approaches to the cellular functions of polyamines in mammals.
AUTHOR: Janne J.; Alhonen L.; Pietila M.; Keinanen T.A.
CORPORATE SOURCE: J. Janne, A.I. Virtanen Inst. for Molec. Sci., University of Kuopio, PO Box 1627, FIN-70211, Kuopio, Finland. Juhani.Janne@uku.fi
SOURCE: European Journal of Biochemistry, (2004) Vol. 271, No. 5, pp. 877-894. .
Refs: 167
ISSN: 0014-2956 CODEN: EJBCAI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
022 Human Genetics
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Apr 2004
Last Updated on STN: 12 Apr 2004
AB The polyamines putrescine, spermidine and spermine are organic cations shown to participate in a bewildering number of cellular reactions, yet their exact functions in intermediary metabolism and specific interactions with cellular components remain largely elusive. Pharmacological interventions have demonstrated convincingly that a steady supply of these

compounds is a prerequisite for cell proliferation to occur. The last decade has witnessed the appearance of a substantial number of studies, in which genetic engineering of polyamine metabolism in transgenic rodents has been employed to unravel their cellular functions. Transgenic activation of polyamine biosynthesis through an overexpression of their biosynthetic enzymes has assigned specific roles for these compounds in spermatogenesis, skin physiology, promotion of tumorigenesis and organ hypertrophy as well as neuronal protection. Transgenic activation of polyamine catabolism not only profoundly disturbs polyamine homeostasis in most tissues, but also creates a complex phenotype affecting skin, female fertility, fat depots, pancreatic integrity and regenerative growth. Transgenic expression of ornithine decarboxylase antizyme has suggested that this unique protein may act as a general tumor suppressor. Homozygous deficiency of the key biosynthetic enzymes of the polyamines, ornithine and S-adenosylmethionine decarboxylase, as achieved through targeted disruption of their genes, is not compatible with murine embryogenesis. Finally, the first reports of human diseases apparently caused by mutations or rearrangements of the genes involved in polyamine metabolism have appeared.

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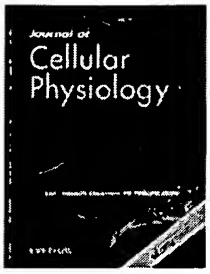
ACCESSION NUMBER: 2004047501 EMBASE
TITLE: Molecular-biological problems of drug design and mechanism of drug action: Metabolism of L-arginine (A review).
AUTHOR: Granik V.G.
CORPORATE SOURCE: V.G. Granik, Res. Inst. Organ. Semiproducts Dyes, State Sci. Ctr. of the Russ. Fed., Moscow, Russian Federation
SOURCE: Pharmaceutical Chemistry Journal, (2003) Vol. 37, No. 3, pp. 111-127. .
Refs: 118
ISSN: 0091-150X CODEN: PCJOAU
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Feb 2004
Last Updated on STN: 12 Feb 2004
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L4 ANSWER 61 OF 61 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:545619 BIOSIS
DOCUMENT NUMBER: PREV199698559919
TITLE: Induction of apoptosis by excessive polyamine accumulation in ornithine decarboxylase-overproducing L1210 cells.
AUTHOR(S): Poulin, Richard [Reprint author]; Pelletier, Georges; Pegg, Anthony E.
CORPORATE SOURCE: Dep. Physiol., Lab. Molecular Endocrinol., Laval Univ. Med. Res. Cent., 2705 Laurier Blvd., Ste. Foy, PQ G1V 4G2, Canada
SOURCE: Biochemical Journal, (1995) Vol. 311, No. 3, pp. 723-727.
ISSN: 0264-6021.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Dec 1995
Last Updated on STN: 28 Feb 1996

AB Deregulation of polyamine transport in L1210 cells overexpressing ornithine decarboxylase leads to a lethal accumulation of spermidine. We now provide evidence that overaccumulation of natural and synthetic polyamines, but not putrescine, rapidly induces apoptosis, as shown by hyper-condensation of peripheral chromatin and internucleosomal cleavage, followed by nuclear fragmentation. Polyamine oxidation is not responsible for the apoptosis observed. Thus, abnormally high polyamine pools could be an important physiological trigger of apoptosis.



Journal of Cellular Physiology
Volume 121, Issue 3 , Pages 476 - 482
Published Online: 4 Feb 2005

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Article

Treatment with α-difluoromethylornithine plus a spermidine analog leads to spermine depletion and growth inhibition in cultured L1210 leukemia cells

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ABSTRACT

Of the three biological polyamines, putrescine (Put), spermidine (Spd), and spermine (Spm), the relevance of Spm to cell proliferation has yet to be defined because of our general inability to deplete it selectively in intact cells. In the present study, Spm depletion was accomplished by treating cultured L1210 cells for 96 hr with α-difluoromethylornithine (DFMO) and an analog of Spd such as aminopropylcadaverine. N^4-methylSpd, N^4-ethylSpd, or homoSpd. DFMO, a specific inhibitor of ornithine decarboxylase, halts continued polyamine biosynthesis and the Spd analog serves as a functional substitute for Spd. Thus, while the Spd analog fulfills the role(s) of Spd in cell proliferation, Spm becomes steadily depleted. In cells treated with DFMO plus the analog, aminopropylcadaverine, Spm pools decline steadily and growth inhibition occurs after 48 hr (when Spm pools decline to 60% of control). By 96 hr, Spm is ~ 15% of control and growth is < 30%. Prevention studies with exogenous polyamines confirm a causai relationship between Spm depletion and growth inhibition. The critical levels of polyamines for cell proliferation to take place were found to be 30% of control for Spd and 60% for Spm. The use of DFMO plus a Spd analog is proposed as a system for studying the cellular consequences of Spm depletion. Spd depletion can be achieved for comparison purposes by treating cells with DFMO alone.

Received: 28 February 1984; Accepted: 29 June 1984
DIGITAL OBJECT IDENTIFIER (DOI)

10.1002/jcp.1041210305 About DOI

Note: Performing your original search, ***methylspermidine***, in PubMed will retrieve ***21*** citations.

All: 1 Review: 0

1: Bioorg Khim. 2004 Jul-Aug;30(4):441-5. Related Articles, Links

[A new synthesis of alpha-methylspermidine]

[Article in Russian]

Grigorenko NA, Vepsalainen J, Jarvinen A, Keinanen TA, Alhonen L, Janne J, Kritsyn AM, Khomutov AR.

A five-step synthesis of alpha-methylspermidine (1,8-diamino-5-azanonane), the first polyamine analogue preventing pathological consequences of spermidine depletion in transgenic rats overproducing spermine/spermidine N'-acetyltransferase, from ethyl 3-aminobutyrate was achieved in a high overall yield.

PMID: 15469020 [PubMed - indexed for MEDLINE]

Jun 21 2006 12:14:26

J. Med. Chem., **49** (1), 399 -406, 2006. 10.1021/jm050872h S0022-2623(05)00872-1
Web Release Date: December 15, 2005

α-Methyl Polyamines: Efficient Synthesis and Tolerance Studies in Vivo and in Vitro. First Evidence for Dormant Stereospecificity of Polyamine Oxidase

Aki J. Järvinen,†‡ Marc Cerrada-Gimenez,†‡ Nikolay A. Grigorenko,§ Alex R. Khomutov,§ Jouko J. Vepsäläinen,*| Riitta M. Sinervirta,† Tuomo A. Keinänen,† Leena I. Alhonen,† and Juhani E. Jänne†

Department of Biotechnology and Molecular Medicine, A.I. Virtanen Institute for Molecular Sciences, and Department of Chemistry, University of Kuopio, Kuopio, Finland, and Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, Russia

Received September 4, 2005

Abstract:

Efficient syntheses of metabolically stable α-methylspermidine **1**, α methylspermine **2**, and bis-α,α'-methylated spermine **3** starting from ethyl 3-aminobutyrate are described. The biological tolerance for these compounds was tested in wild-type mice and transgenic mice carrying the metallothionein promoter-driven spermidine/spermine N^1-acetyltransferase gene (MT-SSAT). The efficient substitution of natural polyamines by their derivatives was confirmed in vivo with the rats harboring the same MT-SSAT transgene and in vitro with the immortalized fibroblasts derived from these animals. Enantiomers of previously unknown 1-amino-8-acetamido-5-azanonane dihydrochloride **4** were synthesized starting from enantiomerically pure (*R*)- and (*S*)-alaninols. The studies with recombinant human polyamine oxidase (PAO) showed that PAO (usually splits achiral substrates) strongly favors the (*R*)-isomer of **4** that demonstrates for the first time that the enzyme has hidden potency for stereospecificity.

Day : Thursday
Date: 6/22/2006
Time: 17:40:30

PALM INTRANET

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EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	5	methylspermidine	US-PGPUB; USPAT	OR	OFF	2006/06/22 20:59
L2	238	514/675.ccls.	US-PGPUB; USPAT	OR	OFF	2006/06/22 21:01
L3	1	l2 and spermidine	US-PGPUB; USPAT	OR	OFF	2006/06/22 20:59
L4	7626	spermidine	US-PGPUB; USPAT	OR	OFF	2006/06/22 20:59
L5	2065	l4 and polyamine	US-PGPUB; USPAT	OR	OFF	2006/06/22 20:59
L6	1807	l5 and spermine	US-PGPUB; USPAT	OR	OFF	2006/06/22 20:59
L7	146	514/631.ccls.	US-PGPUB; USPAT	OR	OFF	2006/06/22 21:15
L8	1	l7 and spermidine	US-PGPUB; USPAT	OR	OFF	2006/06/22 21:04
L9	4126	spermidine	USPAT	OR	OFF	2006/06/22 21:04
L10	1385	l9 and spermine	USPAT	OR	OFF	2006/06/22 21:04
L11	1241	l10 and treatment	USPAT	OR	OFF	2006/06/22 21:04
L12	755	l11 and polyamine	USPAT	OR	OFF	2006/06/22 21:04
L13	142	514/674.ccls.	US-PGPUB; USPAT	OR	OFF	2006/06/22 21:15
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L17	9	l16 and (methylspermidine or methylated)	US-PGPUB; USPAT	OR	OFF	2006/06/22 21:22
L18	22	"5516807"	US-PGPUB; USPAT	OR	OFF	2006/06/22 21:23
L19	1	"5516807".pn.	US-PGPUB; USPAT	OR	OFF	2006/06/22 21:23
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S81	7	methylspermidine	US-PGPUB; USPAT; DERWENT	OR	OFF	2006/06/22 17:58

EAST Search History

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S86	392	S85 same methyl	US-PGPUB; USPAT; DERWENT	OR	OFF	2006/06/22 18:28
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S90	0	aminopropyl adj methyl adj butylamine	USPAT	OR	OFF	2006/06/22 18:44
S91	0	3-aminopropyl adj2 methyl adj2 butylamine	USPAT	OR	OFF	2006/06/22 18:45
S92	5	3-aminopropyl adj2 methyl same (butanediamine or butylamine)	USPAT	OR	OFF	2006/06/22 18:45
S93	3	S88 and methylspermidine	USPAT	OR	OFF	2006/06/22 18:59
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S98	2	"5242947".pn.	USPAT; DERWENT	OR	OFF	2006/06/22 19:37
S99	1	(methyl or methylated) adj spermidine	USPAT; DERWENT	OR	OFF	2006/06/22 19:37